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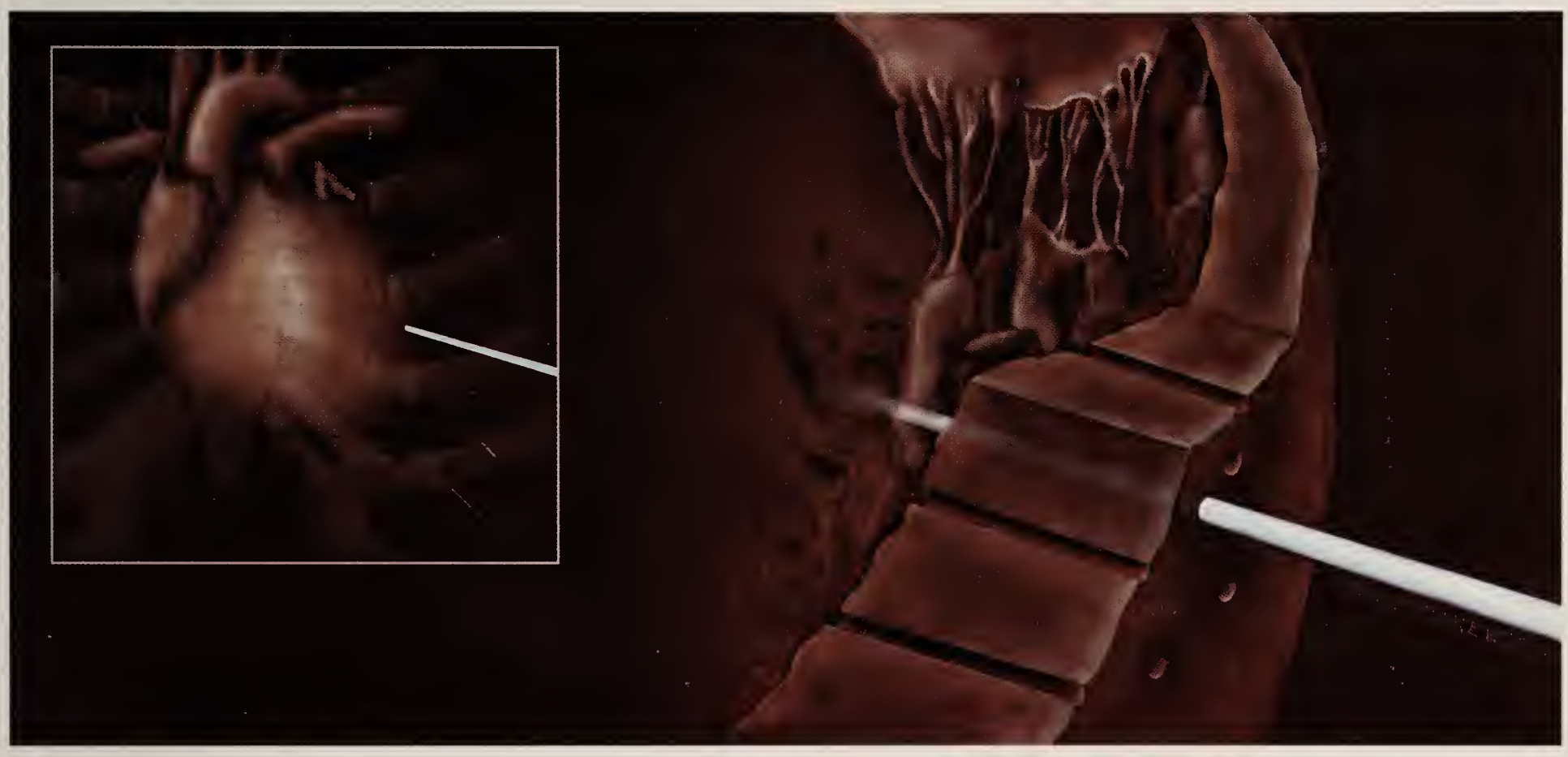

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Editorial

Welcome to the third and final issue of this year's *UTMJ*. Our hearts are a little heavy as our tenure here draws to a close. But the sadness is tempered by a sense of satisfaction and pride as we reflect on the *UTMJ's* successful 75th year of publication. But first we will give you an abbreviated tour of the mystery that lies within the pages of this year's final issue.

The articles in this issue reflect the broad areas of interest of the University of Toronto's medical students. Our feature article describes a new experimental therapy which uses laser-induced destruction of the myocardium in the management of angina. This futuristic technology sharply contrasts the following original article which describes the practises of mothers in Surmang, Tibet, who struggle with even the most basic understanding of diarrheal disease in their infants. The second original article published in this issue details the use of the hospital emergency rooms by Toronto's homeless population.

We also have two practical review articles, one is a thorough literature review of the approach to diagnosis and treatment of thyroid disorders, and the other outlines chemoprophylaxis for opportunistic infection in people with HIV. Both articles will likely be well thumbed by students and staff. Our final article is controversial and reviews a new phenomen termed "Delayed Neonatal Death," which generated a response in Letter to the Editors.

Clinicopathological Correlation and Quick Diagnosis, will challenge, stump, and befuddle many estute students, as usual. Morning Report, a welcome addition to the *UTMJ* and a favourite with students at all levels of training, walks through a belt bustin' presentation of ascites. For all you softies for nostalgia, *From the Archives* finishes up a look at the final 25 years and highlights the artistic metamorphosis of the *Journal* throughout its 75 years of publication.

Working with the staff of the *UTMJ* has been an enriching experience. We are deeply indebted to everyone's hard work, enthusiasm, and common goal to make the *UTMJ* an excellent publication. Thanks must be extended to authors and contributors to the *Journal,* without whom this big ol' plane wouldn't get off the ground. Finally, we thank the generous donation of the patrons and the Medical Society, whose lifeblood financial injection has kept our *UTMJ* hearts beating for another year.

We are confident that next year's staff will take as much pride in the *UTMJ* as we do. Our formation of a UTMJ Senior Advisory Committee and Mission Statement will certainly get them going, and ensure a bright future for Canada's oldest student-run medical journal. It has been a wonderful experience. Don't forget to check us out on the web: http://icarus.med.utoronto.ca/mjweb/www.mjweb.htm.

Sincerely,

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Letter to the Editors

Over the last 50 years, there has been a significant decrease in the neonatal mortality rate. This has largely been due to advances in neonatal care including neonatal resuscitation and the establishment of the modern neonatal intensive care unit for both premature and term infants. There also has been an overall decrease in the infant mortality rate (i.e. the death rate of infants between 1 month and 1 year of age). Even though the overall infant mortality rate has decreased, there is no question that the survival of low birthweight and very low birthweight infants has given rise to a subpopulation at increased risk for infant mortality. This can be related to complications of prematurity itself. The specific factors that lead to increased risk of infant mortality include chronic lung disease and increased risk of sudden infant death syndrome (SIDS). There is no question that low birthweight and very low birthweight survivors of neonatal intensive care units place an increased burden both on the families and society. Of note, not all graduates in the neonatal intensive care units are infants of extreme prematurity and therefore, at risk for these complications. A large number of infants in the neonatal intensive care units have short periods of ventilation for lesser degree of lung disease and there is also a population of children in the NICU receiving care for other medical or surgical problems. These children are at much lower risk for the long-term sequelae described in the article by Weizman (this issue, page 186), and make up a significant proportion of infants in the NICU's.

It is agreed that tracking the long-term sequelae of children in the neonatal intensive care units is at times difficult. This is attempted through neonatal follow-up programs. There would be some advantage from an epidemiological standpoint in changing the definition with regard to mortality numbers for tracking neonatal outcomes. However, it would be important to have this occur on a broad scale, as epidemiological data involved with mortality is collected at many levels (i.e. provincial, national, etc.), as well as being compared on an international basis.

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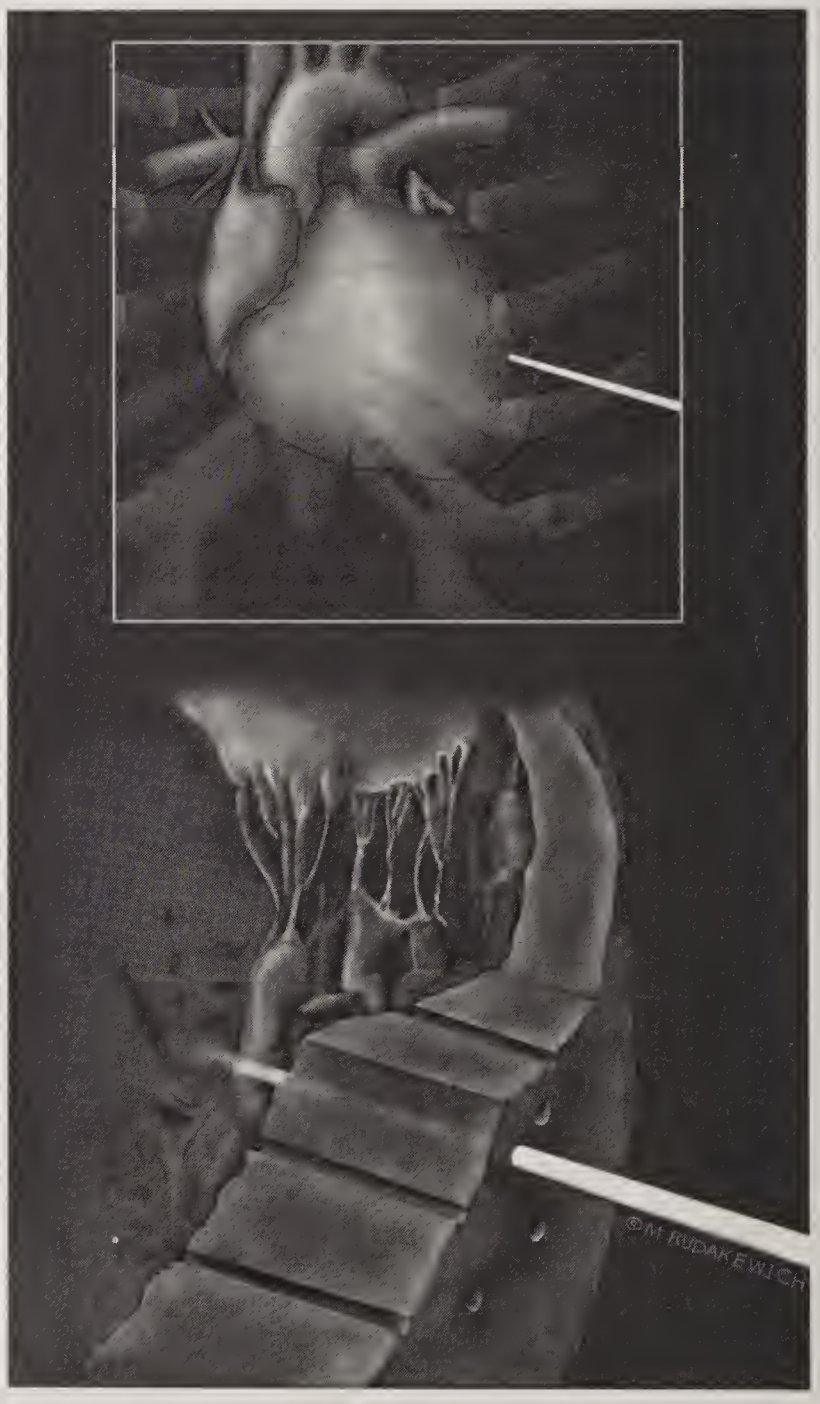
Transmyocardial Laser Revascularization

Andrew J. Lustig, BSc. (OTO) and
Robert J. Cusimano,* BSc., MSc., MD, FRCS (C), FACS

Abstract

Transmyocardial laser revascularization is a relatively new procedure in which high-power laser energy is used to create channels in ischemic myocardium to improve perfusion. The original concept was based on the anatomy of the reptilian heart in which the myocardium is perfused by channels connecting the myocardium to the inside of the heart chambers. It now appears as though transmyocardial laser revascularization does not operate on the principles of the reptilian heart as originally thought. Although the mechanisms by which the procedure works are not understood, patients do report an improvement in anginal symptoms after the procedure. Additionally, the technique leads to a significant improvement in perfusion of those parts of the myocardium treated by laser compared to those not treated. At present, the procedure is suitable for patients with severe angina which is refractory to medical therapy who have contraindications for the more traditional therapies of coronary artery bypass grafting, percutaneous transluminal coronary angioplasty and transplantation. This review article discusses the historical background of the procedure and reviews the existing evidence for and against the procedure. It also discusses several potential mechanisms by which the procedure may work and how the procedure may evolve in the future.



Myra Rudakewich

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Introduction

Before the development of cardiopulmonary bypass facilitating surgery on the arrested heart, efforts were made to treat ischemic heart disease via the creation of extra-coronary sources of blood.[1] The best known and most widely investigated of these attempts was that of Vineberg (1954)[2] who attempted to reperfuse ischemic myocardium by implanting the internal thoracic arteries directly into the myocardium of the left ventricle. In 1965, Sen[3] devised a procedure called transmyocardial acupuncture in which the wall of the left ventricle was punctured to create channels which, it was hoped, would revascularize the heart. It was based on the anatomy of the reptilian heart, in which a network of intramyocardial sinusoids deliver intraventricular blood to the myocardium, thus removing the complete reliance on the epicardial coronary arteries. For this reason, the procedure was dubbed the "snake heart" operation. The original investigators reported a decrease in infarct size and mortality. However, the introduction of coronary artery bypass grafting (CABG) by Favaloro,[4,5] and Johnson[6] in 1969 revolutionized the treatment of coronary artery disease (CAD) and relegated transmyocardial acupuncture to the dustbin of history, at least temporarily.

Currently, the mainstays of the treatment of myocardial ischemia are CABG and percutaneous transluminal coronary angioplasty (PTCA). Despite the success of these interventions, however, many patients are not appropriate candidates because of diffuse or distal coronary vascular disease or lack of a conduit for CABG. It seems that these patients are most likely to benefit from indirect methods of myocardial revascularization such as transmyocardial acupuncture.

The area of transmyocardial acupuncture lay dormant until the development of laser energy sources in the 1980s when several investigators[7] were motivated to revisit the procedure with the new found tool of laser energy. The rediscovery of the technique, now named transmyocardial laser revascularization (TMLR) has been accompanied by a flurry of interest and investigative activity. In TMLR, a narrow laser beam (1 mm in diameter) is used to puncture multiple holes in the beating heart.

In preparation for TMLR, the patient is placed in a 45° right lateral decubitus position. A left anterolateral thoracotomy is performed through the fifth or sixth intercostal space, depending on the location of the point of maximum impulse.[8] The location for the laser drilling is chosen based on the areas with reversible ischemia as indicated by ^{99m}Tc-sestamibi scan. In most of the clinical experience reported in the literature to date, a 1000 W CO_2 laser has been used. However, some surgeons report using a holmium:yttrium-aluminum-garnet (YAG) laser.[9] The CO_2 laser light is not visible to the human eye so helium-neon laser guidance is used for aiming. The laser is fired into the epicardium. It is timed to fire on the 'R' wave of the electrocardiographic cycle when the ventricle is maximally distended with blood and electrically quiescent. This minimizes the probability of precipitating an arrhythmia. The beam penetrates the entire thickness of the ventricular myocardium and is then absorbed by the blood in the ventricle. This can be visualized by transesophageal echocardiography during the procedure as bubbles formed by photomolecular disruption of elemental gases by the laser energy. The channels generated by the laser are 1 mm in diameter and are often arrayed in a distribution of approximately one per square centimeter. Bleeding from channels can almost always be controlled with finger pressure, or in rare instances, by an epicardial suture. A CO_2 laser was initially chosen for TMLR because it has a wavelength of 10.6 μm which is highly absorbed by water, an abundant constituent of soft biologic tissue such as myocardium.[10]

The power of the lasers used for TMLR are approximately an order of magnitude greater than those typically used in other applications in medicine. This represents the first clinical application of laser sources similar in power to those used in material processing such as large-scale cutting and welding of metals.[10]

Results

Despite the controversy over the long-term TMLR channel patency, there seems to be fairly good agreement that the technique is effective at providing patients with symptomatic relief. In some people this benefit is seen almost immediately postoperatively.[1] However, it is not clear whether the beneficial effects from the procedure stem from the channels themselves or from a subsidiary adaptation elicited by other components of the laser-induced response.[11] It is conceivable that the laser energy causes changes at the genetic level which ultimately result in symptomatic changes. In one multicentre series which used TMLR as the sole therapy in 200 patients not suitable for CABG or PTCA, angina class decreased significantly from before treatment to 3, 6, and 12 months after treatment ($p < 0.001$). The procedure carried a perioperative mortality of 9%. In those surviving, however, single photon emission computed tomography (SPECT) perfusion scans revealed a significant decrease in the number of perfusion defects in the treated left ventricular free wall. The subjects also benefited from a significant decrease in angina class and in the number of hospital admissions for angina.[12] In addition ^{99m}Tc-sestamibi scans before and after TMLR have revealed that the technique leads to a significant improvement in perfusion of those parts of the myocardium treated by laser compared to parts not treated.[8] Left ventricular wall motion of lased segments of the myocardium is also observed to improve after TMLR.[13]

In another study in which 55 patients were evaluated at six months after TMLR, it was found that approximately 10% of patients did not benefit at all and were classified as non-responders and an additional 10% of patients died during the perioperative period.[16] Paradoxically, although the remaining 80% of patients did realize improvements in Canadian Cardiovascular Society angina class at one year following surgery, they suffered a small but statistically significant decrease in left ventricular ejection fraction.

At present it is generally felt that TMLR should be

reserved as a 'last chance' option in patients with severe angina pectoris.[16]

Histologic Studies

There is a great deal of controversy in the literature regarding the length of time that TMLR channels remain patent. In fact, it is not even clear if channel patency is even necessary in order for clinical benefit to be realized. Early studies using an ovine model of myocardial infarction were promising because histologic analysis of laser treated infarcts revealed patent channels surrounded by viable myocardium.[14] Although the walls of these channels were devoid of endothelium, there was evidence of blood flow through the channels.

Unfortunately, subsequent studies in humans were not nearly as encouraging. Histologic findings in post-mortem specimens of patients who have previously undergone TMLR indicate that by and large the laser channels do not remain open. Cross sections of myocardium from a patient who died within one week of TMLR reveal cylindrical areas lacking myocytes, yet filled with freshly clotted material including fibrin, erythrocytes and leukocytes.[15] The diameter of the cylinders is 1 mm; the same as that of the laser beam. The cylinder is surrounded by a narrow area of carbonization which is in turn surrounded by a zone of necrosis which extends out to 500 μm on each side of the channel.

In a specimen taken from a patient who died 3 weeks after TMLR, granular tissue was found in abundance. Large numbers of monocytes and macrophages were found phagocytosing the necrotic material within the channel.[15] Numerous active fibroblasts transforming the area into scar tissue were found. Endothelialized, patent, laser-created channels could not be observed in myocardium.[16] The tissue remodeling observed corresponds to the different stages of wound healing.

It must be remembered that the patients whose tissue is available for histological analysis after TMLR are an extremely biased sample because they are the patients who died following surgery. In contrast, in animal studies the hearts of all the subjects are examined. Thus, the observed difference in channel patency between humans and sheep may stem from species differences or it may be a result of the bias in the human tissue examined. It is conceivable that there are differences in the response to laser treatment between human responder and non-responder myocardium.[16]

Proposed Mechanisms

The exact mechanism by which transmyocardial laser revascularization may improve perfusion and thereby provide angina relief is unknown.[8] The original idea behind TMLR was to mimic the physiology of myocardial perfusion in reptile hearts by creating channels for blood to flow from the ventricle into the myocardium.[17] Strangely, the literature on TMLR is replete with mention of human myocardial "sinusoids" which form a trabecular network throughout the myocardium. These sinusoids, it is hypothesized, bathe the myocardium in oxygenated blood from the left ventricle. Although the existence of such sinusoids is well established in several organs including the liver, spleen and bone marrow, they have not been shown to exist in myocardium.[18] The concept of these myocardial sinusoids seems to have originated with Wearn in 1933.[19] This was based on the misconception that there were no thebesian vessels in the left ventricle. It was probably based on extrapolation from more primitive vertebrate hearts in which the myocardial sinusoids are vital to cardiac perfusion.[18] Although remnants of the myocardial sinusoids can be seen in some mammals such as dogs and rabbits, their irregular distribution makes their physiological relevance doubtful.

Interestingly, one 1997 study of a patient who had died after TMLR treatment with a holmium:YAG laser revealed the existence of what the authors describe as "naturally occurring subendocardial sinusoids."[9] These sinusoids were observed to be surrounded by circular zones of viable myocytes.

Obviously, the absence of randomized, controlled trials of TMLR leaves it open to the criticism that its benefit is due to a placebo effect. Although this is a plausible explanation for the post-procedure improvement in angina, it seems less likely to be capable of explaining the more objective observation of increased myocardial perfusion after TMLR.

Several other possibilities exist to explain the symptomatic relief. One is the stimulation of angiogenesis as a result of delivery of laser energy to the myocardium. It is also possible that the laser leads to partial denervation of the heart (with or without revascularization) which plays a role in alleviating anginal symptoms.[12]

One intuitively appealing explanation is that ischemic tissue is forced to derive its energy from anaerobic glycolysis instead of oxidative phosphorylation. However, as lactate accumulates as a by-product of glycolysis, the rate of further glycolysis diminishes. If lactate could be drained away, the reasoning goes, then glycolysis could continue to supply the myocardium with the high energy phosphate bonds it needs for survival. The laser channels, even though they become clogged with granular and then scar tissue, may be permeable to interstitial fluid and permit the washout of lactate and supply of glucose as a substrate for glycolysis.

Future Directions

TMLR is regarded by some as a "high-tech Vineberg." The long term patency of laser channels has not been convincingly demonstrated. To date, no study has been completed with a randomized control group. Currently, two separate multicentre randomized control trials are underway comparing TMLR to medical management and to reoperative CABG. These studies are currently accruing patients and the results are pending.[12] It seems that a great potential future use of TMLR is in conjunction with CABG in patients in whom some territories are graftable and others are not.[12] If proven effective, it may be combined with minimally inva-

sive CABG to provide a way to get around the incomplete revascularization of the myocardium which sometimes results from the minimally invasive approach. In fact, in one series[21] patients with double and triple vessel disease who were unsuitable for conventional CABG had beating heart CABG performed on their left anterior descending (LAD) or right coronary artery and TMLR performed on the area of the heart nourished by the left circumflex and posterior descending coronary arteries. The patients in this study realized marked improvements in angina class, exercise tolerance and reversible ischemia. However, because of the uncontrolled nature of the study, it is impossible to determine what proportion of the clinical benefit was derived from CABG *versus* TMLR. Nonetheless, the hybrid approach is an interesting and promising idea. The first case of TMLR performed with a holmium:YAG laser through a thoracoscopic approach was reported in 1997 and the patient's angina class improved from class III to class I.[22] The holmium:YAG laser is amenable to the thoracoscopic approach because the beam is transmitted through a flexible lightweight optical fiber that can be easily manipulated through the thoracic ports. Preliminary work is now beginning in a therapy called percutaneous endocardial laser revascularization in which a holmium:YAG laser is introduced percutaneously and the channels are drilled moving from the inside of the heart outwards. This therapy would obviate the need for sternotomy or thoracotomy and may be combined with other percutaneous techniques such as PTCA.

One strategy is to augment the clinical benefit of the laser generated channels by simultaneously delivering genes or proteins which promote angiogenesis and endothelial cell motility.[23] In one study, vascular endothelial growth factor (VEGF), a major angiogenic inducer, and the gene encoding human profilin, which increases endothelial cell motility and adhesion, were injected into pigs undergoing TMLR. Unfortunately, these interventions were found to stimulate more inflammation but not angiogenesis.

In conclusion, although the mechanism remains to be elucidated, the preponderance of evidence suggests that patients do benefit clinically from TMLR. Because of its ability to treat myocardium supplied by diffusely atherosclerotic coronary arteries, it may prove useful in transplant recipients who suffer from diffuse atherosclerosis due to chronic rejection.[24] However, based on the observation that laser-created channels do not remain patent and the nonexistence of the postulated myocardial sinusoids, it is unlikely that the clinical effects of TMLR are based on the principles of the Reptilian heart as was originally thought.[15] It may prove to be an important therapeutic modality in patients with severe angina, which is refractory to medical therapy and reversible ischemia, who have contraindications for the more traditional therapies of CABG, PTCA and transplantation.

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Homeless Access to Primary Care in the City of Toronto

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Abstract

The inner-city emergency department (ED) services a significant proportion of homeless individuals. In order to best serve the needs of this population, it is necessary for emergency care providers to have some knowledge of the trends and indicators that characterize primary care access in the homeless community. A short questionnaire addressing access to primary care services was administered to a sample of 68 homeless individuals at selected shelters over the winter of 1997. It was found that the majority believe they access doctor's offices (41%) or walk-in clinics (40%) most often for their primary care needs, while a significant minority chose the ED (15%). The majority (65%) however, had visited the ED in the past year. These results suggest that although the majority of homeless individuals do not perceive the ED as a general primary care centre, this population does visit the ED much more frequently than the general population.

Introduction

The homeless population is faced with significant obstacles to achieving and maintaining health. They represent a heterogeneous group, including those who live permanently on the street, as well as shelter residents, alienated youth, and the mentally ill. The homeless are subject to a broad range of acute and chronic diseases, intensified by unsuitable living conditions, stress, alcohol and drug dependence, and sociopathic behav-

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iour.[1] Incomplete and fragmentary medical care permits exacerbation of chronic disorders.[1]

As the number of homeless people grows in this country's urban centres, health care facilities are increasingly visited by a growing proportion of these individuals. The emergency department (ED), in particular, is a primary care centre often accessed by the homeless population.[2] In the southeast region of Toronto, in an area of 16 square kilometers, approximately 50,000 people live below the poverty line and about 400 patients visit the three area hospital EDs on a typical day.[3] Homeless adults visit all three EDs.

Rates of use of the ED by the homeless population are high; one study found the average number of individual visits was seven per year, and more than one-third of all patients made two or more visits within two days of each other.[3] Increased visits to the ED can be partly attributed to the higher incidence of injury and trauma faced by the homeless population.[4] However, homeless adults often seek care for complaints that are not life-threatening.[5] The *Street Health Report* of 1992, a general survey of homeless individuals living in the city of Toronto, reported a high level of dissatisfaction with the care received at EDs.[4] Forty-five percent of those visiting the ED felt that their problem was not being taken seriously and

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A When you are sick or need medical advice, where do you go most often?
a) doctor's office
b) community walk-in clinic
c) emergency department
d) Street Health

B Have you been to:

A) a doctor's office in the past year	YES	NO
B) a walk-in clinic in the past year	YES	NO
C) an emergency department in the past year	YES	NO
D) Street Health in the past year	YES	NO

C Where would you go first if you:

A) have a bad cold
a) doctor's office
b) community walk-in clinic
c) emergency department
d) Street Health
e) N/A

B) want a check-up
a) doctor's office
b) community walk-in clinic
c) emergency department
d) Street Health
e) N/A

C) want a pregnancy test or want a test for STD
a) doctor's office
b) community walk-in clinic
c) emergency department
d) Street Health
e) N/A

D) for a rash or scabies
a) doctor's office
b) community walk-in clinic
c) emergency department
d) Street Health
e) N/A

E) for alcohol or drug intoxication or withdrawal
a) doctor's office
b) community walk-in clinic
c) emergency department
d) Street Health
e) detox centre
f) N/A

D Do you have a family doctor? YES NO

Name: Location:

Do you have a health card? YES NO

If NO, do you or someone else have a record of the number? YES NO

FIGURE 1. *Primary care access questionnaire administered to participants in study.*

almost a quarter of those visiting the ED left feeling that their problem was not taken care of adequately.[4] This combination of frequent visits and high dissatisfaction has broad implications. It suggests that the health-care needs of this population are not adequately serviced in the ED setting, and reveals a mismatch of patients' agendas and the health services provided. It also has economic implications because increased usage of EDs may contribute to increases in health-care costs and ED overcrowding.[6-9]

The ED at St. Michael's Hospital (SMH) is an emergency care centre visited often by homeless individuals. The SMH ED sees approximately 35,000 patient visits annually, providing twenty-four hour emergency medical services in the heart of downtown Toronto. Its catchment area includes the region described above, and it also is one of two adult trauma centres servicing Metropolitan Toronto and surrounding areas.

To begin to address some of the issues outlined above, we administered a short questionnaire to homeless individuals staying in overnight shelters, hoping to document health care access patterns in this population.

Method

A short questionnaire was designed to address three different components of health care utilization. The first question addressed which of four types of primary health care facilities a person used most often: a doctor's office, a walk-in clinic, the ED, or Street Health (Figure 1a). Street Health is a community-run nursing station program specifically aimed at the homeless population in downtown Toronto. It maintains nursing stations at selected drop-in centres and shelters.

The second part of the questionnaire addressed health services actually utilized. Each interviewee was asked if he or she had visited a specific care centre at least once in the past year (Figure 1b). The third part addressed where an individual believed they would go for care for certain specific health conditions (Figure 1c). The choice "N/A" was reserved for any response that did not include visiting a specific care centre, such as, "I would treat myself," or, "I would never have that problem." Also included was a question on Ontario Health Card possession (including whether or not one had access to a record of his or her health number if he or she did not possess the actual card) and a question on whether or not the individual had a family doctor (Figure 1d). The study was approved by the Research Ethics Committee at St. Michael's Hospital.

The questionnaire was piloted in the ED at SMH on five patients who reported having no fixed address on admission. Slight adjustments were made to the questionnaire to improve the wording in order to remove ambiguity after reviewing the results of the pilot study.

Four sites were chosen for the administration of the survey and approval was received from all four. These sites included The Out of The Cold homeless shelter program at St. Michael's Hospital and at Blythwood Church, situated in North Toronto. The Out of The Cold Program provides overnight shelter for the homeless population during the winter months; various sites operate across the city. Street Haven, a permanent women's shelter, and Seaton House, a permanent men's shelter, both located in the southeast region of Toronto, were also chosen for the study.

The questionnaire was administered to willing participants who were staying overnight at the shelters. Individuals were initially approached by one of the authors (J.W.) or a shelter staff member. While the survey itself was done anonymously, the name and date of birth of the participant were recorded separately in order to avoid repeat participation in the study. The same person (J.W.) administered the questionnaire verbally to all participants.

Results

A total of 68 individuals participated in the study; there was 100% completion of the survey form. Forty-nine men and 19 women took part. Thirteen interviews were conducted at Street Haven, 17 at St. Michael's, 18 at Blythwood Church, and 20 at Seaton House (Table 1).

Table 1
Site Breakdown

Site	Men	Women	Total
SMH	14	3	17
Blythwood	15	3	18
Street Haven	0	13	13
Seaton House	20	0	20
Total	49	19	68

The majority of individuals in the study chose "doctor's office" or "walk-in clinic" as the most frequently utilized centre (Figure 2). Fifteen percent of the sample identified the ED as the most often utilized centre. Very few chose Street Health.

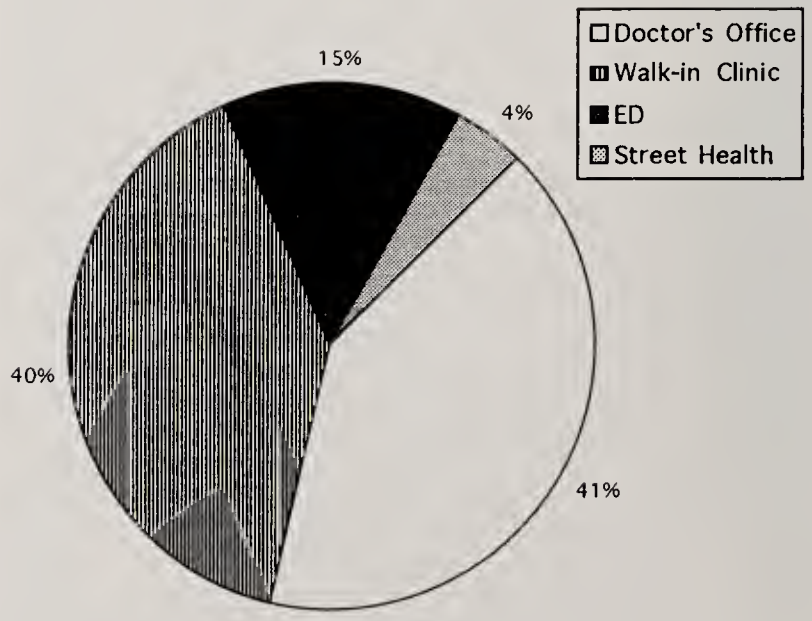

FIGURE 2. *Pie graph displaying distribution of answers to the question: When you are sick or need medical advice, where do you go most often?*

Concerning actual visits to a primary care centre in the past year, over 70% had visited a doctor's office, 50% had visited a walk-in clinic, and 65% had visited the ED. Only 29% had visited Street Health (Figure 3).

Two-thirds of the sample had family doctors. About 40% of those with family doctors chose a centre other than their family doctor as their most often utilized centre.

Fifty-nine percent possessed health cards. Twenty-six percent did not possess the actual card, but had a record of their health number at a health centre, such as their family doctor's office or the ED. Fifteen percent had no card, no record of the number, and no knowledge of anyone else having a record of the number.

In response to the question of where one would go hypothetically for treatment of a bad cold, the majority would not seek treatment, and 29% would go to a doctor's office (Figure 4). For a check-up, the majority would visit a doctor's office. A similar pattern occurred for pregnancy or STD test. Faced with a rash or scabies, most would visit a doctor's office or a walk-in clinic, but over 20% would visit the ED. For alcohol or drug-related intoxication or withdrawal problems, most would access a detox centre.

Discussion

Because of the barriers faced by the homeless to access care provided at a traditional doctor's office, such as lack of a health card, telephone access needed to make appointments, and issues of transportation, we expected that more of our sample would have chosen the ED and/or walk-in clinics as their primary resource. Walk-in clinics, in fact, were identified just as frequently as a doctor's office as a primary care resource. Perhaps because walk-in facilities do not require appointments, but are still set up to deliver non-emergent care, they are a more popular choice than the ED. It is important to note, however, that 15% of those surveyed chose the ED as their main resource for primary care. The ED is designed primarily to be a care centre for emergency medical illness. This demonstrates a mismatch between health requirements and health resources.

Street Health, a community clinic program run specifically for the homeless population, was consistently the least utilized centre among the sample. Many interviewees had never even heard of the program. Expansion of the Street Health program might help lift some of the burden from the ED. Unfortunately, this would require a financial commitment from the community at a time when such resources are scarce.

Although the majority of our sample did not choose the ED as their primary resource, 65% had visited the ED in the past year. The *Street Health Report* reported that 54.4% of the homeless population had visited the ED in the past year.[4] The 1990 Ontario Health Survey reports that 20% of Metro Toronto's population over 12 years of age had visited the ED in the past year.[8] Even though the majority in our survey did not frequently choose the ED as a source of care, as a group they visited the ED over three times more often than the general population.

On examination of the responses to the questions concerning hypothetical illnesses and health-care needs, it seems that most do not perceive the ED as a source for non-emergent care. Faced with a cold, or wanting a check-up or test, few in our study would choose the ED for treatment. Overall, it seems that our sample perceives that they utilize the ED appropriately.

In our study, 26% did not possess a health card and 15% had no card and no record of their number. This is a potential barrier to health care for homeless individuals, since a health card

FIGURE 3. *Bar graph depicting percentage of visits to primary care facilities by the sample in the past year.*

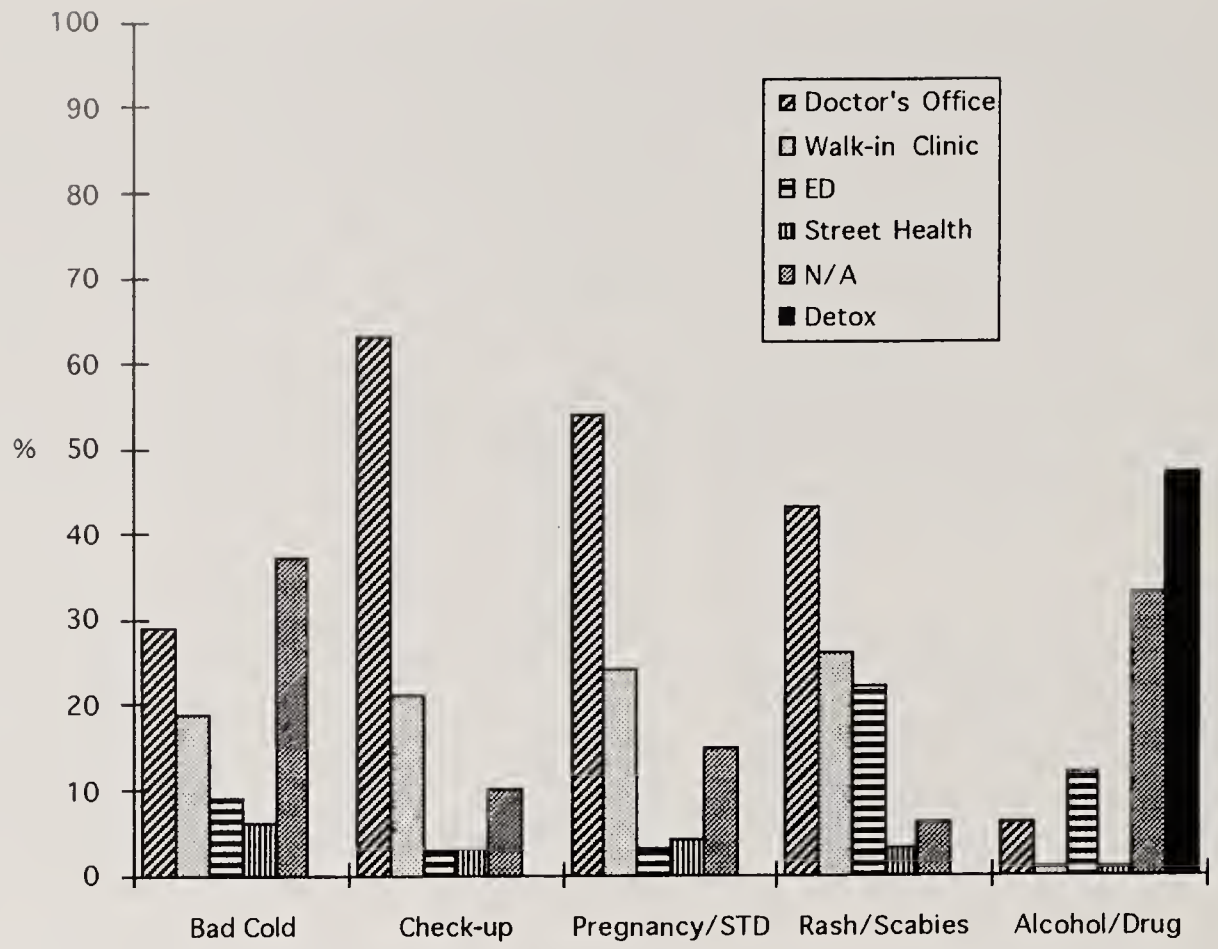

FIGURE 4. *Bar graph depicting percentage of primary care centres hypothetically chosen for certain health conditions/needs.*

is generally required for access to the conventional sources of primary care in Ontario. Those without a card are forced to access centres that are less likely to require a card, such as certain community clinics and emergency departments. Getting a health card can be quite difficult, especially because a birth certificate is required. A major problem in the homeless population is loss and theft of personal belongings and identification, so many no longer possess personal identification.

One limitation of this study is that it relies on the accuracy of self-reported information. No attempt was made to corroborate the survey responses with hospital or clinic information on individual patients.

The study is biased to a certain extent by self-selection. The sample group depended on who was staying at the shelters, and who would agree to participate. Anecdotally, those who appeared in dress and manner more detached from society were less likely to want to participate. This included those who appeared to have psychiatric illness. Also excluded from the study were those individuals who chose not to use the shelters, and instead stay on the street. The inclusion of these groups may have altered the results. Our selection bias was further complicated by the process of data gathering at Seaton House. According to convention at Seaton House, packages of cigarettes were provided to individuals who participated in the study. As well, the staff selected clients they thought would be agreeable and friendly.

In summary, the ED is accessed much more frequently by the homeless community when compared to the general urban population. The ED is not, however, perceived to be a source of primary non-emergent care by most of the homeless community, and the majority indicated that they choose more appropriate centres for non-emergent care. A higher incidence of trauma and other illness requiring emergency care may partly explain increased use of the ED relative to the general population. Further research is necessary in order to better elucidate the reasons for increased ED use by the homeless population so that strategies to decrease unnecessary ED use and improve access to non-emergent primary care facilities can be developed.

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Results of Childhood and Maternal Health Survey, Surmang, Tibet

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Jacqui Shaw

Abstract

Primary health care research in developing countries enables targeting of the populations most in need of help. Currently, two such identified groups are women and children. However, for some areas there is a lack of health information and the needs of these regions are often not known and have never been addressed. In this article, we present the results of a maternal and childhood health survey conducted in one such area, Surmang, Tibet. Twenty-five women with children were interviewed. The results revealed a partly nomadic community in which basic facilities such as running water are not available. Medical care is primarily obtained from Tibetan doctors and there are no clinics or hospitals. Women are uneducated, they work in and outside of the home and have large families. There is no pre- or post-natal care, or trained birth assistants, and there are high pregnancy complication and infant mortality rates. Half the children have had diarrhea, and there was a lack of knowledge about both the risk factors for diarrhea, as well as the appropriate management. Our recommendations are for the conduction of larger studies to confirm and investigate our findings, as well as the implementation of programs that enable these nomadic communities to become relatively self-sufficient rather than reliant on access to specific health care facilities.

Introduction

Every year more and more research is done in developing countries. Estimates of health parameters such as average life expectancy, incidence of childhood disease and malnutrition, and maternal mortality rates demonstrate staggering

results. As a consequence, international conferences have established world-wide maternal and child health goals. Specifically, goals were set to reduce maternal mortality rates by half of 1990 levels and to reduce the under five child mortality rates by 1/3 or to a level of 70 per 1,000 live births (whichever is the greater reduction), by the year 2000.[1] Supporting goals have been set to enable access by all pregnant women to prenatal care, trained attendants during childbirth and referral facilities for high-risk pregnancies and obstetric emergencies, and to reduce by 50% deaths due to diarrhea in children under the age of 5 years and by 25% the incidence of diarrhea. In an effort to reach these goals studies and surveys have been carried out in developing countries to determine current maternal mortality rates, incidence of pregnancy complications, availability of delivery facilities and trained individuals, and pre-natal and post-natal care, along with surveys on childhood illness targeting specifically diarrheal diseases. These surveys have helped local aid projects, relief organisations and larger groups such as UNICEF and the WHO to direct their efforts in the regions studied. This ideally results in targeting the women and children most at need and the pressing maternal and child health problems.

Unfortunately, there are still many areas where even basic maternal and childhood health information is not available. Tibet is one such area. Literature searches done through MEDLINE in advance of this study demonstrated very little published health data. Indeed, much of what is known is from organisations that have begun aid projects in Tibet. One such organisation is Friends of Surmang (FOS). Surmang is a township located in the Yushu County of Tibet, on the border of Qinghai Province and the Tibetan Autonomous Region. Yushu is ranked as number 138 of the 400 poorest counties in China, giving it one of the lowest standards of living in the world.[2] FOS is a non-profit organisation that currently runs a temporary medical clinic in Surmang in the summer months and is presently building a permanent one. From their work in Surmang they have established that the majority of people are extremely poor nomadic yak herders, who are living essentially the same way they have for hundreds of years. They have no access to regular medical care, hospitals or clinics, or schools. There is little use of any currency, and most communities are primarily self-sufficient. Many of the communities have had little or no contact with people that are not Tibetan or Chinese. Very little is known about the health problems of these Tibetan people. The purpose of this study was to conduct a survey of maternal and childhood health in Surmang in order to generate results that might help direct future medical efforts in this and other similar regions of Tibet.

Materials and Methods

Prior to arriving in Tibet a literature search of previously published maternal and childhood health surveys was performed.[3-5] From this literature search and the information from FOS, a survey was designed. The survey questions were then reviewed by a Tibetan interpreter to ensure both that they would be understood by Tibetan women, and that they were culturally sensitive.

A. Survey Design

The survey had three major sections; demographics, maternal health, and childhood health. The maternal health section dealt specifically with pre-natal care, post-natal care, and pregnancy complications. If a woman had more than two children, she was asked to answer the questions with regard to her first and last pregnancies. These women were also asked if any of the other pregnancies had been complicated or different in any way. If the answer was yes (which in fact it never was), the questions would also have been asked about this pregnancy to avoid missing any possibly complicated pregnancies. With respect to the child health component, the mothers were asked about the occurrence of different illnesses in their children under 11 years of age, and were assessed for risk factors for diarrhea. For mothers whose children had experienced diarrhea, the women were asked whether children had been breastfed during the episodes, whether fluid and food intake had been increased, decreased or unchanged and what treatment had been sought for relief of the episode.

B. Population Selection Criteria

There were two criteria used in selecting the women to be interviewed. First, they had to live in the Surmang region, and second, they had to have been pregnant at least once. However, there were two exceptions made to these criteria. These were surveys that were answered by grandmothers in place of their daughters, who were away herding yaks. It was decided that since these grandmothers had lived with daughters, assisted them at their deliveries, and taken care of the grandchildren, that they would be able to adequately answer the survey questions.

C. Region Selection Criteria

The population sample was obtained by visiting the accessible encampments and villages within an approximately fifteen kilometre radius of the Surmang monastery, and interviewing all the women present who fulfilled the criteria. No women refused to be interviewed and the survey was administered to twenty-five women, with data collected on 43 pregnancies, and 45 children. The survey was conducted in the summer of 1996, through a Tibetan interpreter. Where possible the women were interviewed alone. However, sometimes the husband or another woman would be present and would assist in clarifying questions when the interpreter's dialect was different from that of the woman being interviewed. Each interview took between two and three hours to complete.

Results

A. Demographic and Socioeconomic Indicators

The average age of the women interviewed was 33, with a range of ages from 23 to 55 (Table 1). They had on average 3.36 children, and 75% were married, while 25% were single. The average age at first pregnancy was 22. The youngest pregnancy was at age 17, and the latest pregnancy occurred at age 48. The majority of women (72%) worked both in and outside the home as farmers, herders, or both. None of them were able to read or write any language fluently.

Table 1
Demographic and Socioeconomic Indicators

Indicator	Qualifier	Percentage (%)
Age	15-25	20
	26-35	48
	36-45	20
	46-55	12
Marital Status	Single	24
	Married	76
Age at first pregnancy	15-25	80
	26-35	20
Ability to read or write	None	88
	Little	12
	Fluent	0
Occupation	None outside home	28
	Farmer	32
	Herder/nomadic	16
	Both (herder & farmer)	24
Number of children	1	24
	2	32
	3	12
	4	8
	5+	24

Table 2
Living Conditions for Women in Surmang, Tibet

Indicator	Qualifier	Percentage (%)
Living situation	Tent only	0
	House only	52
	Tent and house	48
Availability of running water or electricity	None	100
Availability of designated W.C.	None	92

With respect to their living conditions, approximately half of them lived in a stone hut in the winter and a tent in the summer (Table 2). No women had running water or electricity, and only two had a designated washroom facility (toilet pit).

B. Present Level of Health Care

Almost all (96%) of the women interviewed had seen a doctor before. This was usually a Tibetan doctor (75%), although approximately 20% had seen a Western doctor, and 6% had seen a Chinese doctor. Most women had seen Tibetan doctors in their village or encampment, while the Western doctors had been seen at the temporary clinic set up by FOS, and the Chinese doctors were seen at a hospital. Approximately 60% of women thought they had been immunized in the past, but none were sure of the type of immunization.

With respect to their children, just under 70% had seen a doctor. Again this doctor was usually Tibetan. Immunisation rates for the children were much lower, with at most 40% of children who had been immunised.

C. Attitudes Towards Medical Care

Although the majority (64%) of women interviewed would see a doctor first if they were sick, about one third (32%) would seek help from both a doctor and a lama, and 4% would seek help only from a lama. They were all willing to seek care outside of their community if feasible, and none of them said they would be uncomfortable doing this. The majority (almost 70%) indicated that they would have no preference as to what type of doctor (Tibetan, Western or Chinese) they received treatment from, while 12% would want to see a Tibetan doctor, 8% would want to see another type of doctor, and 12% did not know what their preference would be.

D. Pre- and Post-Natal Care

The data gathered for forty three pregnancies indicated that during approximately half of these pregnancies, the woman had seen a doctor. The most common reason was for non-specific stomach pain (71%). Other reasons were cough (14%), dizziness (10%), and other (5%). After delivery, about three-quarters of women (77%) had seen a doctor, this time, most commonly for prolonged fever (64%). Stomach pain (24%) and other (12%) constituted the reasons for the rest of the visits. In no pre or post-natal visits to a doctor was anything specifically done for the woman because she was pregnant, or for the fetus or the newborn child.

E. Details of Labour and Pregnancy Complications

The overwhelming majority of women (91%) had given birth in a stone hut, while 9% had given birth in a tent. They were attended by their mother (58% of the time), by their husband (26% of the time), or by another woman in the community (16% of the time). A doctor or trained birth attendant was not present for any of the deliveries. The deliveries were reported as all being vaginal deliveries with no cesarean sections reported. The most common pregnancy complication was high fever for more than a day (Table 3). This was associated with back pain, painful urination, and swollen, painful breasts (Table 4). Other major findings were a labour of more than 12 hours (16%), swelling of legs, body or face (16%), and a perceived large amount of blood loss after delivery (28%, Table 3).

F. Pregnancy Termination, Infant Mortality and Birth Control

One of the twenty-five women interviewed had experienced an abortion. All women denied ever deliberately ending a pregnancy. None of the women practiced any form of recognized birth control. Nine percent of pregnancies had resulted in a child that died within six months of birth. Therefore, the incidence of perinatal mortality was five out

of 43 pregnancies, or 12%. This result gives a perinatal mortality rate (sum of stillbirths and neonatal deaths per 1,000 births) of 116. None of the women were able to elaborate on the cause of death.

Table 3
Incidence of Pregnancy Complications

Complications	Percentage (%)
Length of labour >12 hours	16
Perceived high fever during delivery	16
Swelling of legs, face or body	16
Convulsions during pregnancy	0
Perceived large blood loss during delivery	7
Perceived large blood loss after delivery	28
High fever >1 day after delivery	51
Cesarian section performed	0

Table 4
Associated Symptoms of Infection with Prolonged Fever Post-Delivery

Associated Symptoms	Percentage (%)
Severe lower abdominal pain	5
Severe lower back pain	95
Pain or burning on urination	18
Swollen or painful breasts	27

G. Childhood Diarrhea

Of the 45 children about whom data was collected, 23 (51%) had experienced diarrheal episodes. The number of episodes ranged from 2 to 36 times a year.

H. Risk Factors For Diarrhea

The identified potential risk factors were assessed in both the children who experienced diarrhea and those who had not. The diarrhea group (n=23) were breastfed an average of 23.3 months ranging from 1 week to 4 years. The non-diarrhea group (n=22) were breastfed an average of 24.8 months ranging from 1 month to 5 years.

The children with diarrhea were from 16 households of which 69% never used boiled water for drinking or cooking. In contrast, in the 15 households of the 22 children without diarrhea, only 60% never used boiled water for drinking or cooking.

With respect to washing of hands by the mother, 69% of mothers in the diarrhea group, and 73% in the non-diarrhea group never washed their hands or covered their food prior to cooking or serving.

One hundred per cent of the children who experienced diarrhea never washed their own hands before eating. In the group without diarrhea only one washed his/her hands prior to eating.

Only two of the total households (25) had a designated toilet pit. Other households used the river and nearby areas as washroom facilities.

I. Actions/Beliefs During Diarrheal Episodes

During these diarrheal episodes, only 44% of mothers continued breastfeeding. Nine of the twenty-three children (39%) were treated with decreased fluid intake, 35% of children had increased fluid intake and the remaining 26% had no changes made. In 57% of cases mothers decreased food intake during the episodes of diarrhea, in 17% food intake was increased and in the remaining 26% there were no changes made.

With respect to treatment, the majority of cases (70%) were seen by a Tibetan doctor for pills. However, in 22% of the cases no care was sought outside the home. Two cases were seen by a Western doctor, and in one of these cases the patient had been seen previously by a lama for blessings as a form of treatment. Oral Rehydration Salts (ORS) therapy was given in one case (by the Western doctor).

Discussion

The purpose of this survey was to obtain baseline data on demographic, maternal and childhood health in the region of Surmang, Tibet. The sample size (25) and region covered (15 km radius) were both relatively small. This was primarily because of limited resources (two interviewers and one interpreter), the inaccessibility of the nomadic encampments due to the terrain, and the length of time each survey took to complete because of the need to explain to the women and the community what the survey was for, the number of questions, and sometimes the dialect differences between the interpreter and the women. Another limitation of this study is that it is based on the reliability of the answers of the women surveyed. In some cases (e.g. questions about where a woman had given birth, or pregnancy complications), there may be social stigmata associated with certain answers that we were unaware of. There are unfortunately no other surveys with which to compare the data obtained, and because of the small sample size, the results are estimates. However, these results still provide some basic information on the maternal and childhood health, and suggest some possible health trends in the region.

A. Demographic and Socioeconomic Factors

Half the women surveyed lived in a stone hut only, and half lived in a tent and a hut at different times of the year. However, given the difficulty in reaching the nomadic encampments, these statistics may suggest a higher level of hut-living than for the population in general because the women in the villages were more accessible. Most women lived in a basic environment in which there is no running water, electricity or adequate sanitary facilities (Table 1), and only two women had a toilet pit. It is interesting that almost

one quarter of the women interviewed were not married. This appeared to be accepted by the communities, and these women usually lived and were supported by their own families. The average number of children (3.34) is high especially considering that the average age of the women was only 33. As none of these women practice any form of recognised birth control, and none is available, it is likely that most will have large families by the end of their childbearing years. Significantly, none of the women are able to read or write fluently which has important implications for the introduction of any health education or care programs.

The vast majority of health care is delivered by Tibetan doctors in the villages and encampments. Although 20% of women had seen a Western doctor, all of these visits had taken place at the temporary clinic set up by FOS. However, since this clinic is accessible only to those living nearby, this statistic is likely not representative of the population at large. Visits to a hospital were virtually non-existent (one case), which may be explained by a lack of knowledge about their existence, and their inaccessibility and expense. With respect to immunization, although 60% of women claimed to have been immunized, the actual number is likely much lower, if in fact any immunization had been carried out at all. There was some confusion with this question as Tibetan doctors frequently give needles and it was not felt that the women always understood the difference. Furthermore, there was no evidence of any immunization delivery program in place, and the women surveyed were only able to indicate that 40% of the children may have been immunized.

It is apparent that Tibetan women frequently (32% of the time) seek help from both a doctor and a lama, illustrating the importance of the Buddhist religion within their health care. However, from questioning the women with respect to their attitudes towards receiving medical care, all women were willing to seek care outside of their community, and the majority had no preference as to the type of doctor they saw.

B. Maternal Health

During pregnancy, about half of the women visited a doctor, most commonly for stomach pain. However, they all denied having any specific physical exams or tests performed, or recommendations given (e.g. diet etc.) because they were pregnant. In otherwords, there was no form of pre-natal care. Most deliveries were reported to have occurred in a hut. However, on further questioning it became evident that pregnant women were excluded from yak herding in the summer in order to stay in the village and deliver their children. At the deliveries, there were no medically-trained individuals present, and mothers (58%), and husbands (26%), provided most of the help. The assessment of pregnancy complications demonstrated relatively high levels of long labour, high fever during delivery, swelling of body, face or hands, large blood losses after delivery and prolonged high fever after delivery (Table 3). Surprisingly, there were no reported cesarean sections. This may be because this practice is not performed by Tibetan doctors, or may be that it is not discussed by Tibetan women. A further study would have to be performed to assess this finding. Also, further questioning of the women who reported complications sometimes revealed that they had experienced the same complications for all of their pregnancies. This suggests that the questions for these women may not have screened for serious complications such as pre-eclampsia, or post-parturm hemorrhage, but instead were simply recording normal aspects of labour. If this is the case, there is a need for women to be educated about pregnancy and labour. No women reported convulsions during pregnancy, a screen for eclampsia. However, this statistic may be biased by the association of eclampsia with increased maternal mortality.

With respect to the most common complication, high fever post-delivery, many women experienced other symptoms such as back pain, pain on urination, and swollen, tender breasts (Table 4) with the high fever. This suggests that the fevers may have been related to infectious processes. The absence of a sanitary environment in the houses or tents, and the probable lack of sanitary precautions during deliveries would lend support to this finding.

C. Infant Mortality

Given the sample size, it is difficult to make any definite conclusions about perinatal and infant mortality. However, the results obtained suggested a 12% incidence of perinatal mortality rates, most of which was due to a high incidence of infant mortality (9%). This may be explained by the lack of pre- or post-natal care, maternal education, access to medical assistance and the high complication rates.

D. Childhood Diarrhea

In the total sample size of 45 children, an overwhelming 51% of children had experienced diarrhea. This value is significantly higher than episodes in industrialized countries, and one must keep in mind the underreporting that may have occurred by mothers who did not identify episodes of diarrhea in their children. When evaluating identified risk factors for diarrhea, there was no significant difference between the non-diarrhea and diarrhea groups, although important trends can be highlighted. Forty percent of the children in the non-diarrhea group drank only boiled water whereas only 31% of the children in the diarrhea group drank boiled water. Also, on average the mothers with children that did not experience diarrhea tended to breast feed longer than those that did experience diarrhea. The lack of statistically significant differences between the two groups may be explained by the small sample size and the possibility that the risk factors identified in other developing countries may not be as significant in this population. However, the high prevalence of diarrhea indicates the need to explore for additional risk factors.

A significant finding in this survey was the lack of knowledge surrounding the management of diarrheal episodes. Only in 35% of cases did mothers know that they should increase fluid intake. Also, in only 44% of cases did mothers continue to breastfeed. These numbers, along with the lack of ORS therapy and the fact that approximately 22%

of the time children were not taken to see a doctor, clearly indicates that education around management of diarrheal diseases needs to be implemented. Though we were not able to quantify the number of childhood deaths resulting directly from diarrheal diseases, this is also an area that requires further investigation.

Concluding Remarks

Living in a country such as Canada, it is hard to believe that there are still places in the world like Surmang, Tibet. The results of this study demonstrated that Surmang is a remote and poor nomadic community, based on farming and yak herding in which there is no running water or electricity, and very few sanitary facilities. Dwellings are either tents or stone huts, with families moving from one to the other with changes in the season. Furthermore, the most important conclusion is that in this area there are a large number of health care needs that are present and are not being addressed.

First, there are no established public health programs or accessible permanent hospitals or clinics. As a result, resources such as immunisations, birth control or other medications are unavailable. There are also no facilities for the very ill.

Second, women have many children, but there are high pregnancy complication and infant mortality rates. This may be explained by the absence of any pre- or post-natal care, or trained birth assistants. Maternal mortality rates were not measured due to the size and nature of the study, however, they would be an important next step in outlining the determinants of maternal health.

Third, there is a high incidence of diarrhea in children, as well as a lack of knowledge on the part of mothers about how to prevent, and how to manage diarrheal episodes. Educational programs and resources such as ORS Therapy are needed to address these issues.

Unfortunately, the nomadic existence of most Tibetan women and their families, combined with their lack of education, will make the implementation of any programs to address childhood or maternal health challenging. However, women at least, appear prepared and willing to seek care, if available, outside of their communities and from a variety of doctors. Our recommendation is to initially address issues of prevention and management of diarrheal diseases, pre-natal and post-natal care, birth control and training of birth assistants. Ideally this would be done within a framework that enables encampments or villages to be relatively self-sufficient rather than reliant on access to any specific clinic. We also suggest the need for additional and more extensive surveys of Surmang and surrounding regions to further elucidate the health care issues of these communities.

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Delayed Neonatal Deaths: Evidence in Support of the Phenomenon

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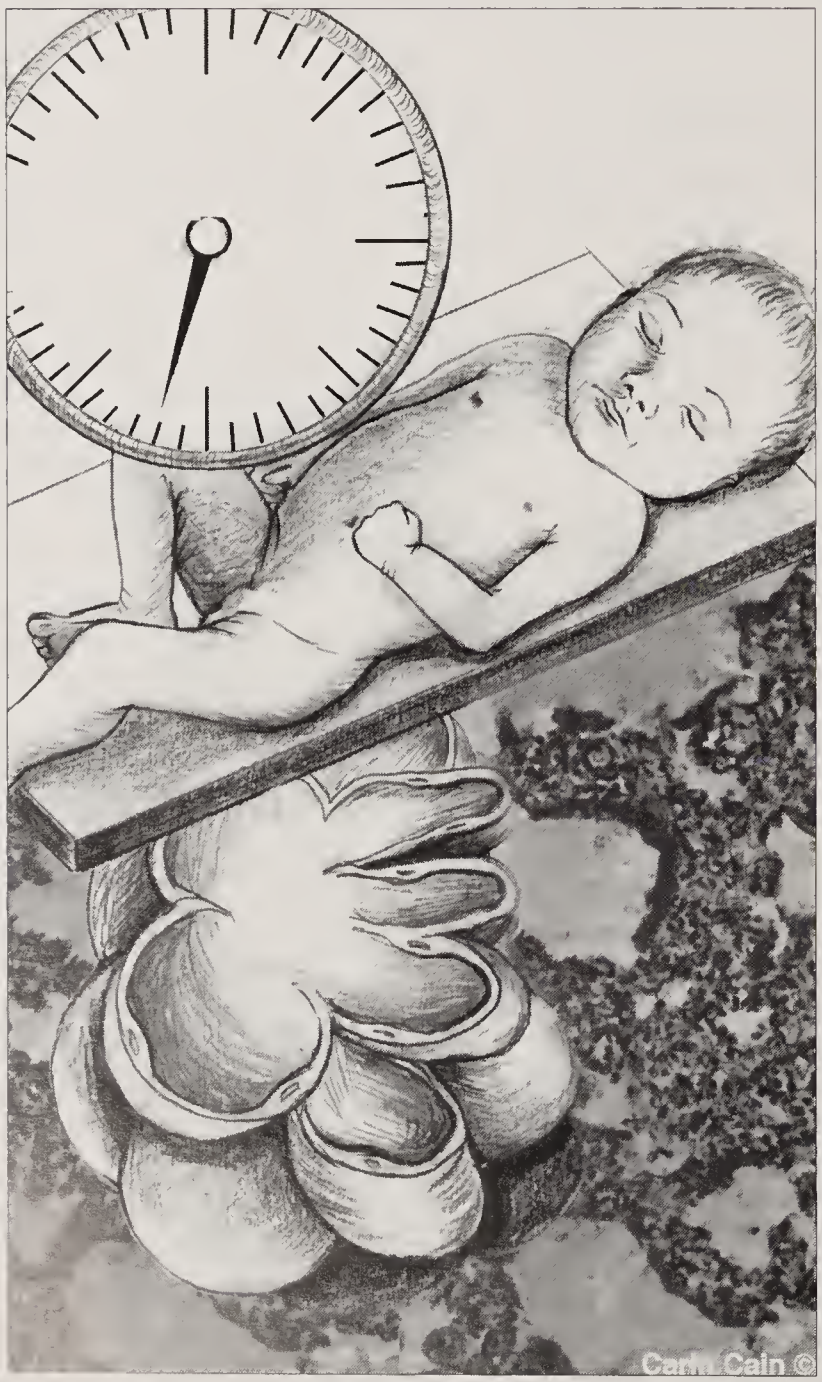

Abstract

The dramatic decline in neonatal mortality associated with the advent of neonatal intensive care units has been well documented. However, the true mortality rate for deaths due to neonatal causes has been underestimated in the literature. It is becoming increasingly apparent that with sophisticated life-support systems, more and more premature, low and very-low-birthweight infants are surviving through the turbulent neonatal period only to die months and weeks later. This paper presents evidence from the literature on the "Delayed Neonatal Death" phenomenon and advocates a new definition of the neonatal period for the purposes of evaluating the true efficacy of neonatal intensive care.

Introduction

Numerous studies have reported the dramatic decline in the mortality rate among the neonatal population over the past 50 years.[1,4] In the United States, the overall infant mortality rate has decreased from approximately 40 per 1000 births in 1945 to 8.4 per 1000 in 1993.[1] This dramatic decline in the infant death rate has largely been attributed to the advent of modern neonatal intensive care.[5] Studies have demonstrated that for the smallest infant, there is an especially pronounced decrease in the risk of mortality associated with level III intensive care centers.[6,7]

It is becoming increasingly apparent that with sophisticated life-support systems, more and more premature, low and very-low-birthweight infants are surviving through the turbulent neonatal period only to die months and weeks later.[4,8-14] This phenomenon of "Delayed Neonatal Deaths" (DND) is marked by a decline in mortality rates during the early neona-

tal period accompanied by a paradoxical lack of decline, or even increase, in late neonatal and postneonatal mortality rates.[8] A Georgian study found two findings indicating this postponement of neonatal deaths: 1) a decrease in postneonatal survival among infants with birth weights of 500 to 999 g and 2) an increase in the proportion of perinatal-related deaths that occurred during the postneonatal period.[1-3] One of the earliest studies of DND, which investigated trends in postneonatal mortality in upstate New York between 1968 and 1979, found a shift toward more deaths at later ages in all weight groups. The greatest changes were found to take place among the lowest birthweight infants with a progressive decrease in the rate of change as birthweight increased.[9] This study found an increase in the percentage of infant deaths occurring in the postneonatal period from 23.1% in 1968-1970 to 27.6% in 1977-1979. Among infants with birthweights between 501-1000 g, postneonatal mortality among neonatal survivors was shown to have doubled over the study period while in the 1001-1500 g range, the percentage of postneonatal deaths was nearly tripled. Infants between 1501-2000 g also showed a doubling in the percentage of postneonatal deaths. Among larger newborns, the increase was not as drastic as those between 2001-2500 g which showed an increase of one-third, and those 2501 g and greater experienced an increase in postneonatal mortality of only 4 percent.[9] Moreover, another study found that 16 of 20 infants dying in hospital beyond the neonatal period did so from conditions directly related to complications of prematurity, such as bronchopulmonary dysplasia, necrotizing enterocolitis, and infection.[8] They found this to be especially true for infants with birthweights between 1001 g and 1500 g, who are the ones that may benefit most from ventilatory assistance, hyperalimentation, and other therapeutic interventions[10] offered by NICUs. In a study conducted in Tennessee, it was found that there was a sixfold increase in postneonatal mortality associated with prematurity-related deaths for very-low-birthweight infants.[11]

The associated pathological conditions of the Delayed Neonatal Death population has been investigated.[14] Of 18 infants whose deaths were categorized as "postponed," all required prolonged artificial ventilatory support and parenteral nutrition. The major findings at autopsy included bronchopulmonary dysplasia, hepatic cholestasis and fibrosis, endochondral ossification, and diffuse cerebral gliosis and infarction. The most common cause of death was infection which has been shown to be common among infants stressed by hypoxia, hyperbilirubinemia, or malnutrition. As well, prolonged catheterization, artificial ventilation, parenteral nutrition, and multiple courses of broad-spectrum antibiotics have been shown to increase the risk for nosocomial and opportunistic infections, especially Candida.[14]

Recognizing the existence of the DND phenomenon and the associated overestimation of neonatal survival rates is significant in light of the financial expenses associated with neonatal intensive care units (NICUs). The increase in survival of neonates due to neonatal intensive care units has been associated with an inevitable increase in medical costs. Neonates in the intensive care nursery have the most expensive of all hospitalized patients.[15] The cost of hospitalization of a low-birthweight infant in an NICU has been found to range from $16000 to $250000 (U.S. dollars).[16] In one study, the average cost of an inpatient day for a non-handicapped child wasapproximately $430, $660 for a mildly handicapped child, and $640 for a moderately-severely handicapped child.[16] In addition, the cost for a congenital diaphragmatic hernia has been shown to be $95000 (U.S. dollars) per survivor who did not receive extracorporeal membrane oxygenation (ECMO) and $26000 (U.S. dollars) per non-ECMO, non-survivor.[15]

The discovery of this phenomenon of Delayed Neonatal Deaths has led to a call for the reconsideration of current neonatal reporting mechanisms, particularly for very-low-birthweight babies.[4,9,10,13] Hack *et al.* (1980)[10] have proposed a modified definition of the neonatal period for the purposes of evaluating the absolute efficacy of neonatal intensive care units. This new definition would include the period from birth until hospital discharge. The long-term goal toward increasing overall survival and maximizing the cost-effectiveness of level III neonatal intensive care units may depend mostly on the reduction of the incidence of low-birthweight.[9]

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An Approach to the Diagnosis and Management of Thyroid Disease

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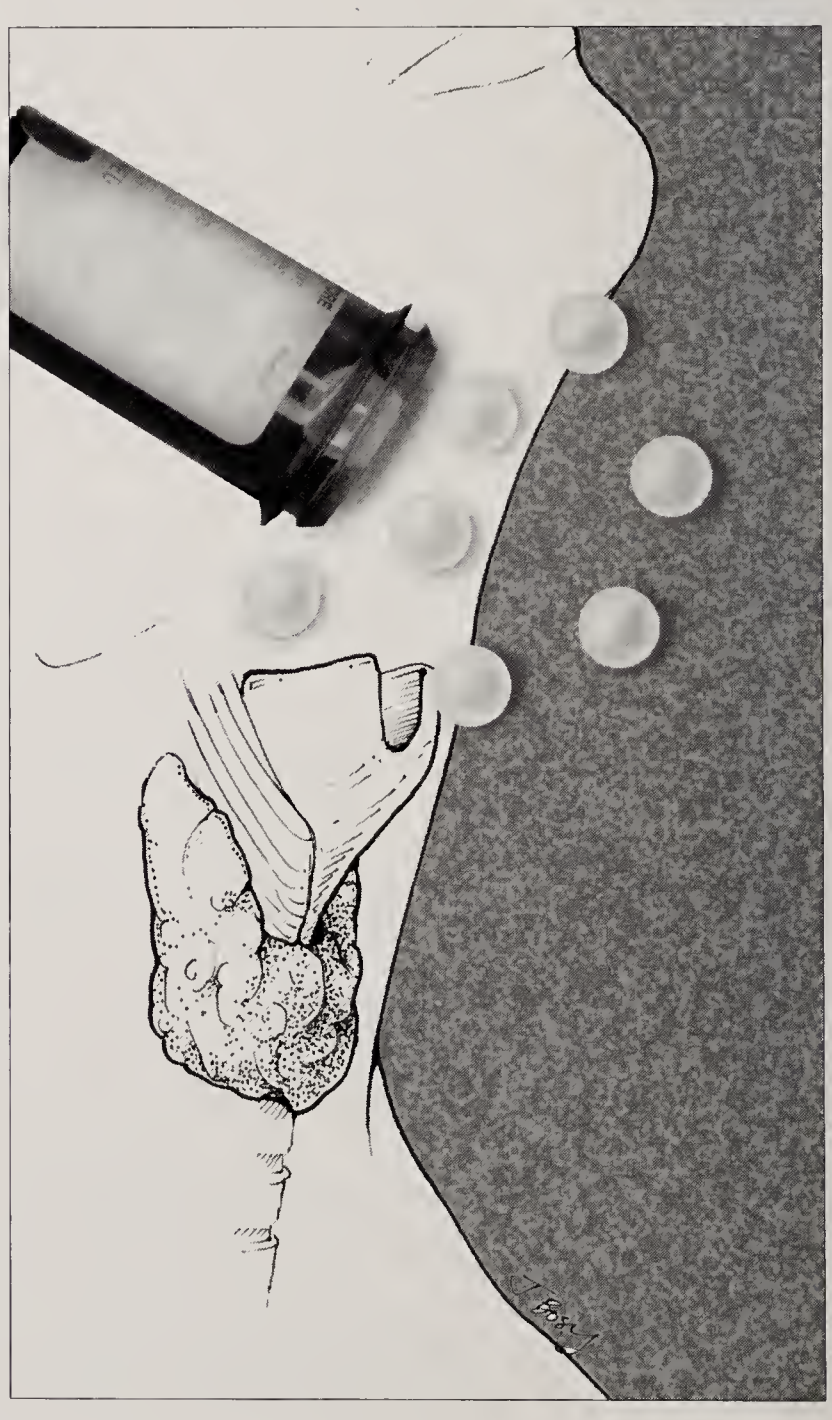
Abstract

Thyroid disease is a common finding in many patients presenting with diverse signs and symptoms affecting many systems. Hyper or hypofunction of the thyroid gland leads to aberrant levels of triiodothyronine and thyroxine, the key circulating thyroid hormones. A focused medical history and physical examination in conjunction with appropriate laboratory tests starting with a serum thyroid stimulating hormone (TSH) are essential in making the diagnosis of thyroid dysfunction. Hyperthyroidism, most commonly due to Graves' disease, is treated with anti-thyroid drugs, and/or gland ablation by radioactive iodine or surgical methods. Hypothyroidism, also most commonly autoimmune in nature, is currently treated with thyroid hormone replacement therapy. Regardless of the type of thyroid disease, careful therapeutic and symptomatic monitoring is necessary after treatment. The investigation of the thyroid nodule is also an important aspect of thyroid disease. Nodules may occur with generalized thyroid dysfunction or may be an isolated finding in the thyroid examination. A rational and step-wise approach to the investigation of a nodule involves a serum TSH, fine needle aspiration biopsy and isotope scanning. These tests will help to rule out a serious thyroid condition. Although thyroid disease is common, preventative population health screening using TSH to evaluate asymptomatic individuals is not currently recommended.



Jennifer Bosy

Introduction

Thyroid disease is a common condition encountered by physicians. There is a wide spectrum in the presentation of thyroid disease which can make the investigation and management of these patients somewhat confusing. However, thyroid disease is

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easily and effectively diagnosed and treated, provided that some basic principles are followed. This article is a guide to the diagnosis and treatment of hypothyroidism and hyperthyroidism, and helps the reader understand the various laboratory tests and drugs that are the mainstay of treatment. Also included is the investigation and work-up of a thyroid nodule. The ultimate goal is to care for these patients in a cost-effective and clinically appropriate manner.

Table 1
Signs and Symptoms of Thyroid Dysfunction

	Hyperthyroid	Hypothyroid
General	Weight loss with good appetite Heat intolerance	Weight gain with regular diet Cold intolerance
Emotional	Nervousness	Tiredness
State	Fatigue Irritability Highly energetic	Depression Weakness Fatigue
Hair	Fine with hair loss	Coarse with tendency to break
Skin	Warm Changes in pigmentation and texture Increase in perspiration	Coarse, scaling and dry
Eyes	Proptosis, Lid retraction Double vision Change in visual acuity	Puffiness in periorbital region
Thyroid gland	Enlargement, diffuse or nodular	Goiter or nonpalpable gland
Cardiac	Tachycardia Arrhythmia Palpitations	Hypotension Bradycardia
Gastrointestinal	Increased frequency of bowel movements	Constipation
Menstrual/ Reproductive	Decreased menstrual flow	Increased menstrual flow Decreased fertility
Neuromuscular	Increased weakness, especially of proximal muscles Tremor	Lethargy but good muscle strength Delay in deep tendon reflexes

Adapted from various sources.[1-3]

Presentation of the Thyroid Patient

The hormones produced by the thyroid gland, triiodothyronine, (T3) and thyroxine, (T4), exert their effects across many body systems. As a consequence, many varied and seemingly unrelated signs and symptoms may be present in a patient with thyroid dysfunction (see Table 1).[1,2,3] Unlike joint pain or urinary tract symptoms, thyroid disease is unique in that patients rarely present to their physician complaining of specific localized symptoms. Rather, the symptoms are oftentimes of a global nature. As with any medical condition, a proper history, physical examination and appropriate laboratory tests are necessary for accurate diagnosis, work-up and treatment. Tips for a good thyroid examination are presented in Table 2. In some cases, patients may present after noticing a thyroid nodule (a discrete swelling within the gland) or a goiter (a diffuse swelling or mass in the neck corresponding to an enlarged thyroid gland). Nodules and goiters may be present in either hyperthyroid, hypothyroid or euthyroid metabolic states.[4] The investigation of a thyroid nodule is dealt with as a separate issue in this article. However, keep in mind that all patients with suspected thyroid disease, regardless of whether they have a nodule or goiter, should be appropriately investigated.

Table 2
Examination of the Thyroid Gland

Helpful Tips for Examining the Thyroid Gland

- Know your anatomy: The thyroid gland normally lies at the level of the fourth tracheal ring, just below the cricoid cartilage. The cricoid is a few cm below the thyroid cartilage or Adam's apple. The gland may be lower in patients with a kyphosis.
- Anterior or posterior approaches are acceptable but relaxing the sternocleidomastoid on the side being examined is helpful. A slight turn of the head down and towards the side being examined is usually sufficient.
- Have the patient swallow a small amount of water for inspection as well as palpation.
- Attempt to assess the gland for texture, mobility, tenderness and nodularity in addition to overall size.

Etiology of Thyroid Disease

Vanderpump *et al.* (1995) in the Wickham Survey, a 20 year longitudinal study of thyroid disease in a British community, identified thyroid disease as having a prevalence of approximately 10-15% in the adult population. It was also found to be 5-10 times more prevalent in women than men.[5] Key subgroups at risk include post-partum and post-menopausal women. Also at higher risk are the elderly, those with an iodine deficiency, a previous head and neck radiation exposure, and most importantly, those with a strong family or personal history of thyroid or other autoimmune disease.[6]

A. Common Etiologies of Hyperthyroidism (Thyrotoxicosis)

a. Graves' disease, an autoimmune mediated stimulation of the thyroid gland by thyroid-stimulating immunoglobulins (TSI) which bind to TSH receptors.[8] Graves' disease is oftentimes accompanied with ocular involvement (ophthalmopathy) and skin changes. Common eye symptoms include lid lag, a characteristic stare, photophobia, proptosis, diplopia, eye pain, exposure keratitis and a decrease in visual acuity. Skin involvement can take the form of pretibial myxedema, a thickening of the dermis. On physical examination a diffuse and soft goiter is commonly found.
b. Autonomous hyperfunctioning thyroid nodule.[7]
c. Toxic multinodular goiter (Plummer's disease). This is more common than Graves' disease in the elderly.[1] There is no ophthalmopathy or thyroid autoantibodies present.
d. Drug induced, e.g. over-aggressive treatment of hypothyroidism, or drugs containing pharmacological doses of iodine.[9,10,11]
e. TSH secreting pituitary tumour.[12]

B. Common Etiologies of Hypothyroidism

a. Autoimmune destruction of the thyroid tissue such as in Hashimoto's thyroiditis, mediated by anti-thyroid microsomal (peroxisome) antibodies and anti-thyroglobulin antibodies. In

a study by Amino (1976), antithyroglobulin antibodies were reported in about 60% of patients with a diffuse goiter and/or hypothyroidism and antimicrosomal antibodies were found in 95% of cases.[13] On physical examination in Hashimoto's thyroiditis, a rubbery goiter is commonly found which may not necessarily be symmetrical.

b. Previous treatment of hyperthyroidism by anti-thyroid drugs, or surgical/radioiodine ablation of the gland. Studies have placed the prevalence of hypothyroidism at 5-25% after treatment with surgery or antithyroid drugs.[14,15]
c. Drug induced, e.g. medications such as lithium[16-18] and glucocorticoids.[19,20]
d. Hypopituitarism with TSH insufficiency.[6]
e. Idiopathic.
f. Iodine deficiency (rare).[6]

Laboratory Investigations

A serum TSH is the most important laboratory test to determine thyroid function in patients. The American Thyroid Association and the Ontario Medical Association recommend this test as the single entry point for patients with suspected thyroid dysfunction.[1,21-23] When the TSH is normal, the individual can be considered to be euthyroid and further testing is not required unless dictated by clinical judgement.[21] When the TSH is outside the normal range, further confirmation testing is required: a free T4 (FT4) for suspected hypothyroidism, and a free T3 (FT3) and FT4 for suspected hyperthyroidism.[21] These tests will assist in making the diagnosis of primary or secondary thyroid disease as shown in Figure 1.

If Hashimoto's thyroiditis is suspected from a strong family history, anti-thyroid microsomal and anti-thyroglobulin antibodies should be measured.[24] If Graves' disease is suspected, thyroid stimulating immunoglobulins may be measured. This latter test is commonly done for pregnant women suspected of having Graves' disease.[25] Since thyroid stimulating immunoglobulins (TSI's) cross the placental barrier and can stimulate the fetal thyroid *in utero,* high levels predict risk for neonatal hyperthyroidism.[21,26,27] Levels of TSI can also be used to predict relapse after medical treatment of Graves' disease.[8]

Patients who are investigated for hypothyroidism may exhibit a mild or moderately elevated TSH level with a normal FT4. This is referred to as subclinical hypothyroidism and the American Thyroid Association estimates its prevalence at up to 15% of patients older than 65 years of age.[1] As a general rule, these patients are only treated with thyroid hormone replacement therapy if symptomatic.[6] A study by Staub *et al.* (1992) looking at patients with subclinical hypothyroidism indicated that the severity of symptoms was correlated with elevated TSH levels.[28] Careful monitoring of this group is indicated as many of them will eventually go on to develop overt clinical hypothyroidism.[1]

There are many drugs that can alter serum levels of TSH, FT3 and FT4 either by decreasing absorption from the gut, altering serum transport, altering metabolism or by influencing the concentration of thyroid-binding globulin. A specific discussion of these drugs is beyond the scope of this article, however a recent review has been written by Surks and Sievert (1995).[29] Nevertheless, multiple drug interactions should be always considered in any patient who presents with and is being treated for thyroid disease.

Treatment of Hypothyroidism and Hyperthyroidism

Currently, there are very effective treatments for hypothyroidism and hyperthyroidism. However, a patient's thyroid status may change quickly and for this reason, regular reassessment is necessary for effective management.

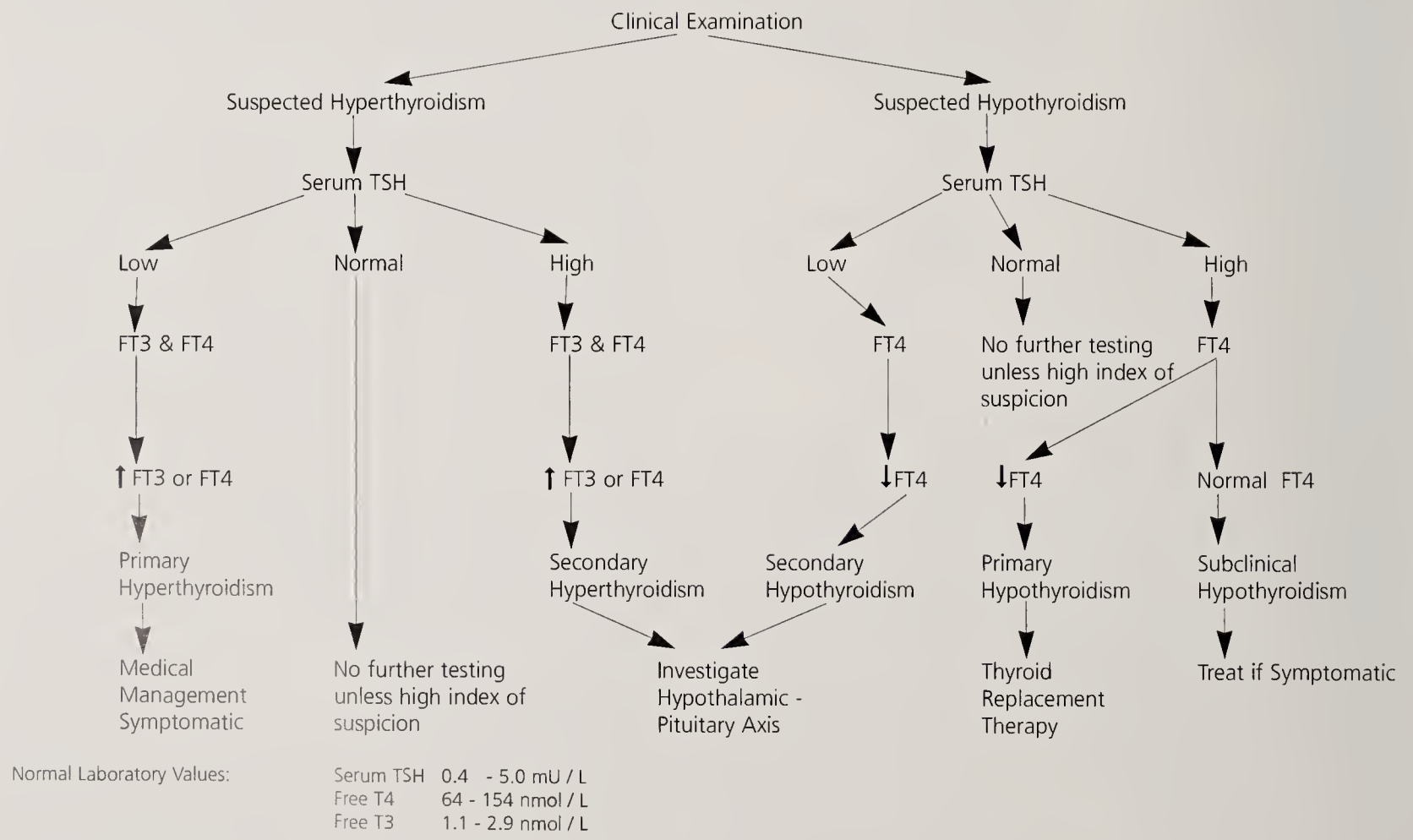

FIGURE 1. Laboratory Investigation of Thyroid Dysfunction.

A. Hypothyroidism

Levothyroxine Sodium, a synthetic preparation of T4, is the preferred treatment for the management of hypothyroidism.[30] Preparations are manufactured in many different doses allowing for the precise titration of an individual patient's requirements. Young adults with hypothyroidism require approximately 1.7 mg/kg of body weight per day for full replacement.[1] Therapy for patients under 50 years of age with no significant medical problems is normally initiated with full replacement. Children may require higher doses up to 4 mg/kg of body weight per day while the geriatric population may require less than 1 mg/kg of body weight per day in order to achieve a euthyroid state.[1] For patients with a history of cardiac disease, regardless of their age, a lower initial dose is indicated which can be increased if dictated by patient symptoms and laboratory investigations. Certain drugs, such as cholestyramine,[31] ferrous sulfate[32] and aluminum hydroxide antacids[33,34] can interfere with levothyroxine absorption from the gut. Other drugs, especially the anticonvulsants carbamazepine and phenytoin[35] may increase levothyroxine metabolism necessitating a higher daily dose. In the initial states of thyroid hormone replacement therapy, clinical and biochemical re-evaluations should be carried out every 6 to 8 weeks until a normalized serum TSH is obtained and symptoms are no longer present. Once normalized, a follow-up every 6-12 months is indicated with a serum TSH measurement at least annually.[1] However, compliance is always an important issue since studies have shown that up to half the patients taking thyroid hormone replacement are lost to follow-up.[7]

Maintenance of normal TSH levels is essential in thyroid hormone replacement therapy as there is some evidence that excessive thyroid hormone levels (and thus low TSH levels via negative feedback mechanisms) cause a decrease in bone mineral density and an increased risk for osteoporosis in postmenopausal women.[36,37] Whether the decrease in bone mineral density induced by levothyroxine replacement actually results in an increased fracture rate however, has been questioned.[38] Thus, subnormal TSH values are inappropriate for hypothyroid patients receiving thyroid hormone replacement therapy and the dose should be reduced until the TSH values return to within the normal range.[39] Some studies also indicate a negative effect of excessive thyroid hormone on the heart including increased heart rate, increased prevalence of cardiac arrhythmias and increased left ventricular mass.[36]

B. Hyperthyroidism

Primary hyperthyroidism can be treated in many ways including pharmacological agents, radioactive iodine (^{131}I) therapy and surgery.

i. Pharmacological Agents

Anti-thyroid drugs such as propylthiouracil and methimazole inhibit thyroid hormone biosynthesis. Typical starting doses are 10-40 mg for methimazole and 100-600 mg for propylthiouracil. Oftentimes anti-thyroid drugs are used before radioactive iodine therapy is initiated.

ii. Radioactive Iodine Therapy

This is the most common form of therapy used in primary hyperthyroidism for patients above the age of 50. It is contraindicated in pregnant or lactating women.[40] Women should have a pregnancy test prior to receiving this treatment and those who receive this treatment, should wait at least six months before becoming pregnant. Treatment with radioactive iodine has not been linked to decreased fertility or an increased risk of cancer. There are also no adverse effects to children born to

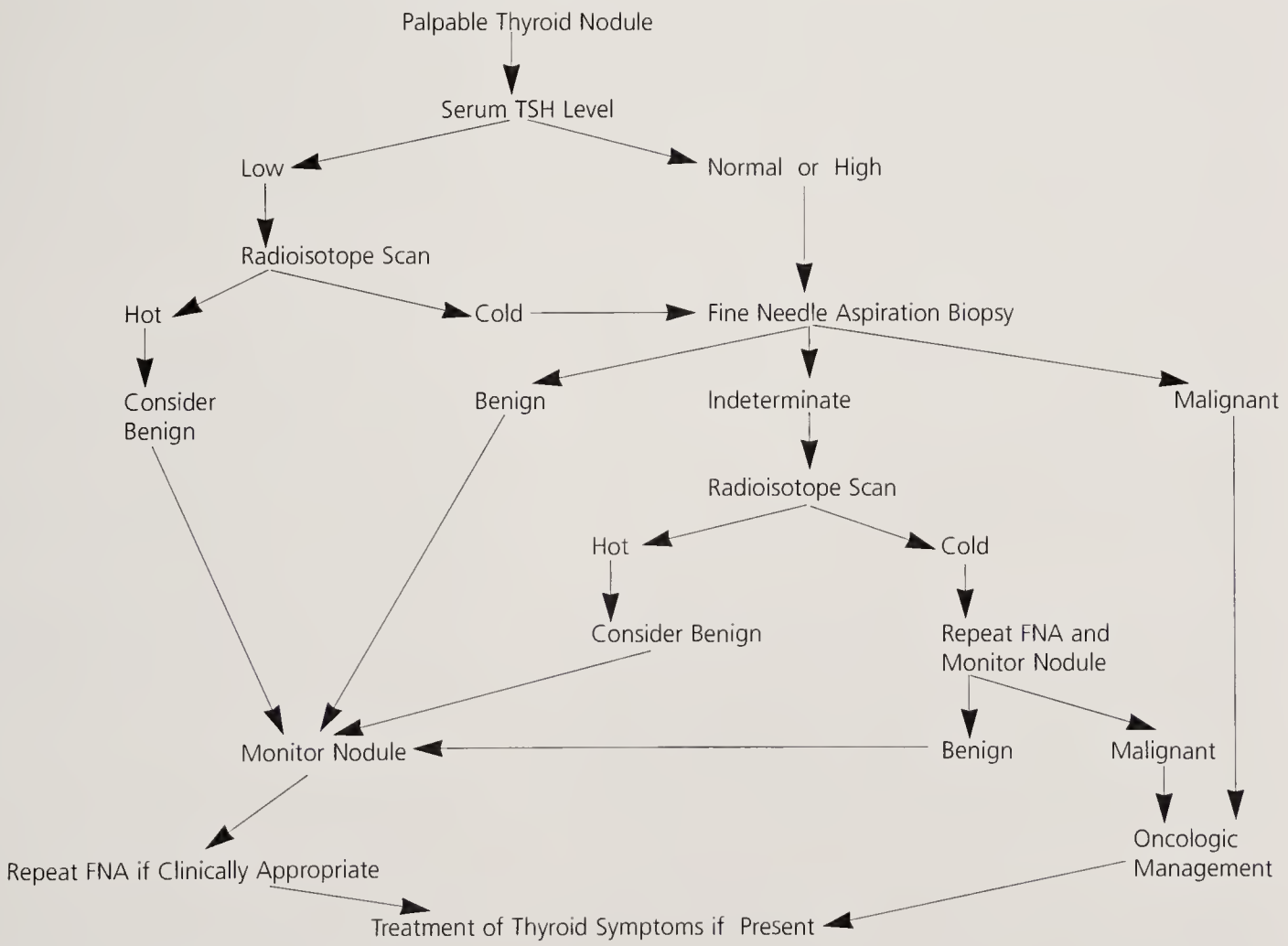

FIGURE 2. Flow Diagram for Investigation of Thyroid Nodule.

mothers who have received I^{131} treatment in the past. This is normally a one time treatment with the principal post-treatment side effect being hypothyroidism, often requiring life long thyroid hormone replacement therapy.

iii. Surgery

Surgical removal of the thyroid gland is an uncommon treatment modality for primary hyperthyroidism. Specific indications may include very large goiters, resistance to ^{131}I therapy or relevant drug allergies.

Adjunctive therapy can be used in hyperthyroid patients in the interim until the euthyroid state is achieved. Most commonly, ß-adrenergic blockers can be employed as required to provide symptomatic relief.[7]

The Thyroid Nodule

A discrete mass or nodule in the thyroid gland may be discovered during a patient's physical examination or less commonly, may be the initial presenting complaint. Among adults, more than 6% of females and approximately 2% of males have palpable thyroid nodules.[41] Typically, the solitary thyroid nodule is a benign lesion,[42] however they are investigated in order to rule out the possibility of a thyroid malignancy.

Nodular thyroid disease includes solitary masses and multinodular glands that may be present in hypothyroid, hyperthyroid and euthyroid states. The frequency of nodular thyroid disease increases throughout life[43] and ultrasound studies show a prevalence of approximately 30-50% in the asymptomatic general population.[44,45] Nodules >1.5 cm in size can be detected upon physical examination and should be characterized for size, consistency, fixation, and associated local lymphadenopathy.[42]

The differential diagnosis of a benign thyroid nodule includes cysts, adenomas, inflammatory thyroid disease (Graves' disease, Hashimoto's thyroiditis), infectious agents, granulomatous processes and congenital abnormalities such as a thyroglossal duct cyst. Malignant thyroid nodules may be primary thyroid cancers (including papillary, follicular, medullary and anaplastic variants), secondary metastases (most commonly from breast and lung) and thyroid lymphomas.

Although the majority of nodules are benign, the following should increase a physician's index of suspicion for a malignancy:[46]

a. rapid nodule growth
b. very firm nodule
c. fixation to adjacent tissue structures
d. vocal cord paralysis or prolonged hoarseness
e. enlarged local lymph nodes

It is generally accepted that all patients with thyroid nodules should be investigated to rule out a malignancy. A generalized approach is shown in Figure 2. The initial work-up includes a TSH measurement and a fine needle aspiration (FNA) biopsy of the nodule. The reported accuracy of cytological diagnosis ranges from 70-97%.[47] Provided that an adequate specimen is obtained, three cytological results are possible - benign, malignant or indeterminate (suspicious) findings.

Definitively malignant nodules are treated with appropriate oncologic management, most often surgical removal of the gland.[48] Benign nodules are followed clinically for changes in nodule characteristics and patient signs and symptoms. A repeat FNA may be recommended in 6 months.[42] Patients with indeterminate FNA results should receive radioiodine scanning of the gland since the presence of a "hot" nodule (a hyperfunctioning area of thyroid tissue) usually indicates a benign lesion.[49] A "cold" nodule should be investigated with a repeat FNA and close clinical monitoring.

Other investigative modalities include ultrasound, and as mentioned previously, a radioisotope scan of the thyroid gland. Ultrasound is useful to categorize nodules as solid, cystic or mixed and is an excellent method to determine the volume of a nodule.[21,42] It is most commonly used to follow changes in benign nodules or in cases of post surgical follow-up. Radioisotope scans, although unnecessary for most patients, may be useful for patients with indeterminate FNA or those with a low serum TSH. Both ultrasound and radioisotope scanning are not reliable modalities to distinguish benign from malignant nodules.[50]

In the work-up of a thyroid nodule, one must always remember to look for and treat hypothyroid or hyperthyroid states if they occur either before, after, or during treatment.

Special Considerations

A. Thyroid Disease and Pregnancy

Graves' disease is the major cause of hyperthyroidism in pregnant women (complicating 0.2% of all pregnancies) and has been associated with preeclampsia, increased fetal loss, premature labour and low birth weight.[26,51] During pregnancy, the course of Graves' disease usually improves due to decreased aggressiveness of autoimmune mechanisms and decreased concentrations of autoantibodies.[52] However, an exacerbation of Graves' hyperthyroidism is usually observed in the post-partum period.[53] In general, any patient treated for hyperthyroidism during pregnancy should be monitored and evaluated closely in the pre- and post-partum period (seen at 4 to 6 week intervals) due to the possible worsening of the hyperthyroidism. Medical management is preferable to surgery or radioactive iodine therapy, and the anti-thyroid drug of choice during pregnancy is propylthiouracil as it crosses the placenta less than methimazole.[1,40] Transplacental crossage of propylthiouracil has been associated with goiter in the fetus.[54]

Hypothyroidism, either before or during pregnancy, also carries several risks including decreased fertility and an increased risk for obstetrical complications such as intrauterine fetal demise, gestational hypertension, placental abruption and poor perinatal outcome.[52,51] The most common causes for hypothyroidism during pregnancy are chronic autoimmune thyroiditis or post hyperthyroid treatment.[7,26] Women who are on thyroid hormone replacement therapy prior to pregnancy require an increase in their daily levothyroxine dose during gestation and a serum TSH measurement is recommended every trimester.[1,52,55] The levothyroxine dose normally returns to the pre-pregnancy dose soon after delivery.

B. Thyroid Disease and the Elderly

As mentioned previously, the prevalence of thyroid disease increases significantly in the elderly, particularly in women. In addition to the pharmacological considerations, there are a few other key points that should be mentioned. In many cases, the elderly hyperthyroid patient may have few if any symptoms and

signs of hyperthyroidism except for weight loss, difficulty in concentrating, and cardiac abnormalities, in particular atrial fibrillation and/or congestive heart failure. Hypothyroidism in the elderly is oftentimes characterized by subtle signs and symptoms that include hoarseness, deafness, confusion, dementia, ataxia, depression, dry skin or hair loss.

Preventative Health Screening

The use of TSH serum assays for widespread population based screening to detect mild thyroid failure in asymptomatic individuals has yet to be widely accepted for use in Canada and the United States. However, a recent decision and cost effectiveness analysis by Danese *et al.* (1996) demonstrated that large scale screening for mild thyroid failure compares favourably with other generally accepted preventative medical practices such as breast cancer screening and estrogen replacement therapy.[56] This study concluded that physicians should consider measuring TSH levels every five years in asymptomatic patients aged 35 years and older undergoing routine health examinations. This recommendation was deemed to be most cost-effective in elderly women. These recommendations have yet to be accepted by the Canadian Task Force on Preventive Health Care or the United States Preventive Services Task Force. Current OMA guidelines suggest using TSH testing only in high risk populations or individuals who exhibit multiple symptoms suggestive of thyroid dysfunction. It is recommended that screening a patient who has only a single non-specific symptom (e.g. fatigue) not be performed.[23]

Conclusions

The diagnosis and management of thyroid disease is made significantly easier when one keeps in mind the varied signs and symptoms with which patients can present. Appropriate laboratory testing helps to pinpoint a primary or secondary cause of thyroid dysfunction. When treating patients for thyroid disease, polypharmacy, other significant medical illnesses and individual variation in age, gender and weight are essential considerations in the initiation and maintenance of therapy. Current treatment modalities are largely successful at eliminating patient symptoms and re-establishing the euthyroid state, allowing patients to live normal and productive lives.

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Primary Care Prevention and Chemoprophylaxis of Opportunistic Infections in HIV Disease

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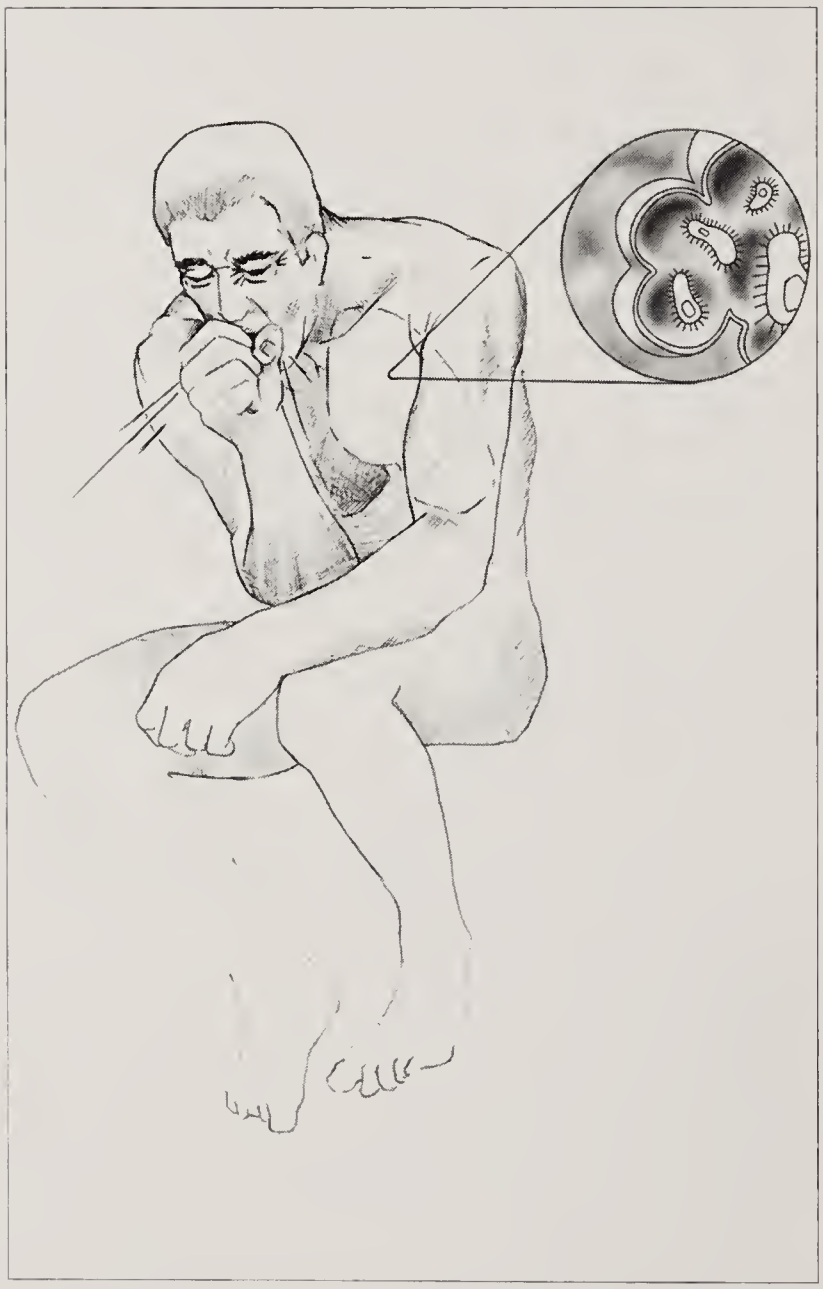

Brett Clayton

Abstract

Opportunistic infection is a major cause of morbidity and mortality in persons infected with the Human Immunodeficiency Virus. In 1997, the United States Public Health Service (USPHS) and the Infectious Disease Society of America (IDSA) published revised guidelines for the prevention of opportunistic infection in HIV-infected individuals. There is evidence to indicate that existing chemoprophylaxis regimens confer a considerable reduction in mortality and extend survival in patients with severe immunocompromise. We review the evidence supporting recommendations for the most common opportunistic infections in advanced HIV disease and consider the implementation of chemoprophylaxis in the primary medical care of HIV-infected individuals.

Introduction

The advent of potent anti-viral therapies has dramatically improved the life expectancy of patients infected with the Human Immunodeficiency Virus (HIV). In the face of the increased life expectancy of HIV-infected individuals, opportunistic infections continue to be a major cause of morbidity and mortality, especially among those individuals who are severely immunocompromised (with CD4+ lymphocyte counts under 200/L). The ever-increasing period of time during which patients are living with advanced HIV disease and immunocompromise demands that the primary medical care of these patients include administration of preventive/prophylactic measures wherever possible.

While the efficacy of trimethoprim/sulfamethoxazole in preventing *Pneumocystis carinii* pneumonia (PCP) has been widely proven and accepted, other prophylactic measures have

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become available in recent years. This article will consider strategies to reduce the incidence of opportunistic infections in patients infected with HIV, considering first primary prevention strategies to reduce exposure to common opportunistic pathogens. This article will also review secondary prevention strategies and the evidence for recommending chemoprophylaxis, particularly the recommendations made by the 1997 Infectious Disease Society of America (IDSA) Guidelines for the Prevention of Opportunistic Infections in Persons Infected with the Human Immunodeficiency Virus.

Primary Care Prophylaxis

In the primary care setting, prevention and prophylaxis should begin with a thorough evaluation of the patient's risk status including history of high-risk behaviours, screening for active disease and relevant serology. If applicable, particular emphasis should be placed on patient education so as to reduce the risk of primary infection.

Chemoprophylaxis of opportunistic disease in HIV-infected patients will comprise a series of steps, with each prophylactic intervention being implemented as the patient becomes susceptible to infections by that particular pathogen. Thus, as a patient's CD4+ cell count progressively drops throughout the course of their disease, the patient should be offered interventions for protection against PCP/toxoplasmic encephalitis, MAC infection, CMV and pulmonary tuberculosis if warranted. Table 1 represents a summary of the various regimens recommended.

Pneumocystis carinii Pneumonia

Pneumocystis carinii is disseminated worldwide, existing in the lower respiratory tracts of a variety of domesticated animals and humans. Although symptomatic infection is rare in healthy individuals, serological studies have indicated that asymptomatic infection usually occurs in most persons by a young age. Prior to the advent of prophylaxis regimens using trimethoprim-sulfamethoxazole, PCP was the most recognized AIDS-defining opportunistic infection. Without prophylaxis, PCP will occur in up to 85% of AIDS patients at some point in the

Table 1
Prophylactic Measures Recommended at Various Levels of Immunocompromise*

Criteria	Pathogen	First Choice	Alternate Regimen
CD4+ count <200/μL	*Pneumocystis carinii*	TMP-SMZ 1 DS tablet daily (AI)	TMP-SMZ 1 DS tablet three times weekly (BIII) dapsone100mg daily (BI) dapsone 50mg daily + pyrimethamine 50mg and leucovorin 25 mg weekly (BI)
CD4+ count <100/μL	*Toxoplasma gondii*	TMP-SMZ 1 DS tablet daily (AII)	TMP-SMZ 1 single strength tablet daily (BIII) dapsone 50mg daily + pyrimethamine 50mg and leucovorin 25 mg weekly (BI)
CD4+ count <50/μL	*Mycobacterium avium* complex	Clarithromycin 500 mg twice daily (AI) Azithromycin 1200 mg every week (AI)	Rifabutin 300 mg daily (BI)
	Cytomegalovirus	Oral ganciclovir 1g three times daily (CII)	
Skin test >= 5 mm induration or Contact with active TB	*Mycobacterium tuberculosis*		
	Isoniazid sensitive	Isoniazid 300 mg daily + pyridoxine 50 mg daily x 12 months (AI)	Rifampin 600 mg daily x 12 months (BII)
	Isoniazid Resistant	Rifampin 600 mg daily x 12 months (BII)	Rifampin 300 mg daily x 12 months (CIII)
	Multidrug Resistant	Consult with local public health department	

**Based on 1997 IDSA guidelines. Evidence supporting recommendations is indicated in brackets.*

course of their illness. The case fatality rate of PCP in these patients is 5-40%. Prior to widespread prophylaxis PCP represented a major cause of death in AIDS, and prophylaxis has been shown to increase survival in these patients.[1]

A. Exposure

Due to the dissemination of this pathogen in the environment, no recommendations for prevention of exposure have been endorsed at this time, although it would seem prudent that PCP patients in hospital be isolated from other high-risk populations.

B. Chemoprophylaxis

The IDSA Guidelines strongly recommend PCP prophylaxis for HIV-infected individuals who have a level of immunocompromise indicated by any of the following markers: CD4+ T-lymphocyte counts of less than 200/μL, unexplained fever of greater than two weeks duration, or a history of oropharyngeal candidiasis.

Several compounds have proven efficacious as prophylaxis against the development of PCP: trimethoprim-sulfamethoxazole, dapsone and pyrimethamine.

i. Trimethoprim-sulfamethoxazole

Trimethoprim-sulfamethoxazole (TMP-SMZ) is the preferred prophylactic agent for PCP. This agent is attractive in that it is widely available and inexpensive. The IDSA Guidelines gave an AI-level recommendation to the regimen of one double-strength tablet daily.[2] Clinical trials have demonstrated high efficacy in the prevention of PCP, with disease incidence while on prophylaxis between 0% and 4%. However, practitioners and patients must be aware of side effects such as rash, fever, neutropenia and nausea, and watchful for the development of hypersensitivity reactions such as the Stevens-Johnson syndrome. These side effects are more common in HIV-infected individuals, and in clinical trials the side effects accounted for about 25% of patients discontinuing prophylaxis.[3]

Regimens that are often better tolerated include one single-strength tablet daily or one double-strength tablet three times a week. The efficacy of these alternate TMP-SMZ regimens is not as well established but appears comparable. It has also been shown in trials that TMP-SMZ possesses ancillary benefits by protecting patients against toxoplasmic encephalitis as well as many other bacterial infections with *H. influenzae, S. pneumonia, Listeria, Shigella, Salmonella* and *Nocardia species.*[4]

ii. Dapsone, Pyrimethamine and Leucovorin

If TMP-SMZ is not tolerated, alternative regimens include daily dapsone and lower-dose dapsone with weekly pyrimethamine and Leucovorin. Addition of the pyrimethamine, a potent antifolate drug, requires the concomitant administration of Leucovorin to protect hematopoiesis. Pentamidine with specified nebulizers can also be used, although an increased incidence of pneumothorax has been documented with pentamidine therapy. These regimens should be considered second-line and were given BI-level recommendations by the IDSA.

Toxoplasma gondii

Toxoplasmic encephalitis (TE) is the second most common AIDS-related CNS infection, and can occur through primary infection or secondary reactivation of latent infection. Primary *Toxoplasma gondii* infection occurs through ingestion of *T. gondii* cysts in soil contaminated by cat feces or ingestion of tissue cysts in undercooked red meats. In states of severe immunocompromise, reactivation of latent tissue cysts in the brain can occur, resulting in toxoplasmic encephalitis. In severly immunocompromised patients seropositive for toxoplasma gondii antibodies, who are at increased risk for disease reactivation, TE occurs in 10-50% of patients.

A. Exposure

HIV-infected individuals who are seronegative for *T. gondii* antibodies should be counselled on measures to prevent primary infection. They should avoid consuming raw meats and practice good handwashing and hygiene following contact with soil, cat litter and feces.[5]

B. Chemoprophylaxis

HIV-infected individuals with CD4+ lymphocyte counts less than 100/μL who are seropositive for *T. gondii* antibodies should be offered TE chemoprophylaxis.

Several regimens have been found effective in prophylaxis of TE: TMP-SMZ, dapsone, and dapsone with pyrimethamine and Leucovorin.

i. Trimethoprim-sulfamethoxazole

The doses of TMP-SMZ used in prophylaxis regimens of PCP appear to be effective in preventing toxoplasmic encephalitis. The regimen of one double-strength tablet daily received an AI-level recommendation from the IDSA. When an HIV-infected patient becomes susceptible to TE (i.e. a CD4+ lymphocyte count < 100/μL), they are usually receiving TMP-SMZ for PCP prophylaxis, so TE prophylaxis has already been instituted.

ii. Dapsone

Fortunately, if a patient cannot tolerate TMP-SMZ for PCP and TE prophylaxis, the other dapsone-containing PCP prophylaxis regimens are also effective in preventing toxoplasmic encephalitis. The alternative regimen of choice is that of dapsone and pyrimethamine plus Leucovorin, which received a BI-level recommendation from the IDSA.

Mycobacterium avium Complex

Mycobacterium avium and *Mycobacterium intracellulare* make up the two most common forms of atypical mycobacteria which form the *Mycobacterium avium* complex (MAC). With the increased survival of severely immunocompromised AIDS patients, MAC has quickly become the most common systemic bacterial infection affecting this patient population.[6]

A. Exposure

MAC bacteria are ubiquitous in the environment, and large

reservoirs of bacteria exist in soil and in various water sources. Despite this, sophisticated studies designed to pinpoint the route of MAC infection failed in 80-90% of cases.[7] Because exposure risks remain ill-defined, there are no primary prevention strategies to reduce exposure that have been clinically proven.

B. Chemoprophylaxis

As with other opportunistic infections, the likelihood of developing infection with *Mycobacterium avium* complex is proportional to the severity of immune compromise, and is thus inversely proportional to a patient's CD4+ count. Following exposure, the MAC burden in an infected patient rises gradually. At CD4+ cell counts between 100 and 400/μL temporary bacteremia often occurs but infection at this time is usually localized. By the time a patient's CD4+ count has declined to less than 10/μL the MAC burden is very high.[8] At CD4+ counts below 100/μL, there is an increased incidence of MAC bacteremia with a 50% increase in the risk of development of disseminated MAC infection. The 1997 IDSA guidelines suggest starting prophylaxis at CD4+ lymphocyte counts less than 50/μL. Whether or not chemoprophylaxis is instituted, patients should receive ongoing clinical surveillance with MAC blood cultures, if clinically indicated.

Three antibiotics have demonstrated efficacy as prophylactic agents against MAC disease: Clarithromycin, Rifabutin and Azithromycin.

i. Clarithromycin

Clarithromycin has become the agent of choice for prophylaxis against disseminated MAC infection, and received a level-AI recommendation as a first-line agent in the 1997 IDSA guidelines. The efficacy of clarithromycin is evident in recent clinical trials where clarithromycin 1000 mg/day conferred a 69% reduction in disseminated infection and a 28% increase in survival. In patients with CD4+ lymphocyte counts less than 100/μL, clarithromycin has also been shown to provide ancillary benefit and decrease the incidence of PCP, community-acquired pneumonia, *Giardia* infection and neoplastic disease.[10] Issues regarding selection of resistant MAC strains have been raised in regards to the long-term use of clarithromycin. The emergence of strains that are resistant to macrolide antibiotics is worrisome as this decreases the number of drug choices for a therapeutic regimen if disseminated MAC infection occurs despite prophylaxis. To address this issue, it has been suggested that prophylaxis be started at a relatively low MAC burden ($<10^9$ MAC bacteria bodywide) so as to avoid the selection of resistant organisms.

ii. Rifabutin

Rifabutin was the first drug to demonstrate efficacy as a MAC prophylaxis regimen in clinical trials and was given a level-BI recommendation in the 1997 ISDA guidelines. Administration of rifabutin was associated with a 25% increase in survival in two clinical trials. Use of rifabutin was not associated with selection of rifabutin-resistant MAC bacteria, although there is a low risk for selecting resistant *M. tuberculosis* strains, so exclusion of active tuberculosis in prospective patients is recommended.[11]

iii. Azithromycin

Azithromycin 1200 mg once a week has demonstrated efficacy similar to clarithromycin in trials (59% risk-reduction of developing disseminated MAC bacteremia) and thus was recommended as a first-line prophylactic agent with an AI evidence rating in the 1997 ISDA guidelines.

Mycobacterium tuberculosis

Mycobacterium tuberculosis is an acid-fast bacillus that, along with the closely related *Mycobacterium bovis,* causes tuberculosis. In North America, tuberculosis tends to be a disease of the elderly, the urban poor, and patients with AIDS. However, in countries where HIV infection is endemic, tuberculosis is the single most important cause of morbidity and mortality in AIDS patients. Tuberculosis is thought to infect approximately one third of the world population and has been estimated to account for up to 6% of all deaths worldwide.

A. Exposure

HIV-infected individuals should be counseled on activities and occupations that carry an increased exposure risk, for example employment in health-care facilities and exposure to homeless populations or correctional facilities. Decisions to continue employment and voluntary activities deemed to be high-risk should include consideration of the prevalence of tuberculosis in the community.

All HIV-infected individuals should receive a tuberculin skin test at the time of diagnosis with criterion for a positive test being induration greater than or equal to 5 mm. HIV-infected persons may have a compromised ability to react to PPD-tuberculin skin testing due to an increased incidence of cutaneous anergy. A multifactorial assessment including cutaneous anergy screening may be helpful in the assessment of a high-risk patient. It should be noted, however, that difficulty in the standardization and reproducibility of anergy testing limits its usefulness, thus it is not recommended as a routine test.[12] Patients with positive skin tests should undergo a clinical evaluation, chest X-ray and sputum culture to rule out the presence of active tuberculosis. HIV-infected individuals who possess symptoms of active tuberculosis should also undergo such evaluation, regardless of their skin test result.

B. Chemoprophylaxis

The ISDA has identified patients with skin test reactions yielding induration greater or equal to 5 mm, or who have had contact with active tuberculosis, to be candidates for chemoprophylaxis. The choice of prophylactic agent depends on the prevalence of drug resistant strains in the community.

i. Isoniazid

For communities with predominantly isoniazid-sensitive strains, a 12 month-course of isoniazid is the recommended regimen. Because HIV-infected individuals are already at risk

for peripheral neuropathy, it is especially important that these individuals also receive pyridoxine for protection against isoniazid-induced neuropathy.

ii. Alternative Regimens

The choice to use alternative prophylaxis regimens should be made on the basis of drug resistance in consultation with the local public health department. For isoniazid-resistant strains, rifampin or rifabutin should be considered. Strains that prove to be multidrug-resistant demand investigation of drug sensitivity and close consultation with local public health authorities. It is important to consider the possible drug interactions of these agents and various HIV-antiviral medications (e.g. rifabutin and protease inhibitors) when choosing an alternative agent.

Patient adherence to chemoprophylaxis is very important in tuberculosis prophylaxis both for efficacy and to quell the development of drug-resistant strains. Whenever possible, direct observation/administration of medications is desirable if patient adherence is in doubt.

Cytomegalovirus

Cytomegalovirus (CMV) is a member of the herpesvirus family and is responsible for congenital infection syndromes, mononucleosis and hepatitis in the general population. Scroprevalence of CMV can be greater than 90% in high-risk patient populations such as injection drug users and males with multiple male sexual contacts. Following reactivation of latent infection, localized tissue involvement includes retinitis, esophagitis and colitis.

A. Exposure

Patients who are members of low-risk groups or who test seronegative for CMV should be warned that CMV is shed in cervical secretions, semen and saliva, and precautions should be taken to reduce the risk of exposure in sexual activity. HIV-infected persons who are also child-care providers or who are exposed to a child-care environment should be warned that they are at greater risk of acquiring CMV infection and should adopt good hygiene and hand-washing practices. Practitioners should also endeavor to transfuse CMV-seronegative patients with CMV-seronegative blood, if possible.

B. Chemoprophylaxis

The natural history of CMV infection consists of three phases: latent infection, reactivation and localized visceral infection. Prophylaxis against visceral CMV infection is indicated during the first phase, which is characterized by low CMV viral loads, in order to prevent reactivation and subsequent localized infection and tissue damage.[13] The 1997 IDSA prophylaxis guidelines have identified HIV-infected individuals who are seropositive and have CD4+ cell counts less than 50/μL as candidates for CMV prophylaxis.

i. Ganciclovir

Currently only oral ganciclovir has been investigated as an agent for prophylaxis against CMV disease. Acyclovir is not effective against CMV and valacyclovir has been found to increase mortality in AIDS patients using it for CMV prophylaxis. One large double-blind randomized control trial demonstrated a 49% reduction in risk of CMV disease including CMV retinitis, colitis and esophagitis with ganciclovir prophylaxis. It was also demonstrated that oral ganciclovir prophylaxis decreased the incidence of lymphoma.[14] However, subsequent studies have yielded conflicting data, and a cost-analysis demonstrated that oral ganciclovir prophylaxis and periodic plasma PCR testing for CMV DNA resulted in very small benefits at huge cost.[15] This has led the IDSA to give CMV prophylaxis a CIII-evidence rating and no specific recommendation on whether or not it should be offered. Periodic fundoscopic examinations and vigilance on the part of the patient in watching for floaters or visual field losses may be equally effective, but less costly interventions. The various side effects of ganciclovir such as neutropenia and anemia must also be considered in the decision of whether or not to implement prophylaxis.

Conclusion

Opportunistic infection remains a major cause of morbidity and mortality in HIV-infected individuals, and defines the Acquired Immunodeficiency Syndrome. The high prevalence of opportunistic infection in these populations demands that primary care of HIV-infected individuals include strategies for the prevention of such infection, both through reduction of exposure and prophylactic measures.

As has been demonstrated, there is sufficient evidence to promote chemoprophylaxis against opportunistic infection as an individual becomes susceptible to such infections due to progressive immunocompromise. The choice of agent will depend not only on efficacy, but also the patient's tolerance to the agent as well as the possibility of interaction with other medications. These strategies of chemoprophylaxis should be combined with patient education to reduce the risk of exposure to pathogens thus reducing the risk of primary infection. Patient education should also include instruction to watch for the onset of clinical symptoms of specific opportunistic infections. Although outside the scope of this discussion, it should be noted that there is an important role for vaccination and the development of active and passive immunities in primary care of HIV patients (e.g. Hepatitis B immunization for those who are susceptible).

The response of HIV-infected patients to new antiviral treatments is manifest in the increasing numbers of HIV-infected patients who are living with varying degrees of immunocompromise, thus facing the threat of opportunistic infection. Prophylactic regimens have been proven to be effective means of preventing such infection and reducing associated morbidity and mortality.

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In the Literature

Tamoxifen and Breast Cancer Prevention

After six years of research, the Breast Cancer Prevention Trial has reported a 45% reduction in breast cancer incidence in high-risk women taking tamoxifen. Breast cancer risk was determined using calculations based on age, number of affected first degree relatives, parity, age at menarche and past history. Investigators released the initial results 14 months ahead of schedule and have notified women in the placebo group so that they might also benefit from the treatment. The trial, which involves over 13 000 women, is being conducted by the National Surgical Adjuvant Breast and Bowel Project in more than 300 centres in the United States and Canada. The researchers found that women taking tamoxifen suffered fewer bone fractures, with no difference in the number of myocardial infarctions between the tamoxifen and placebo groups. Although the results are encouraging, tamoxifen was also found to increase the incidence of endometrial cancer, deep vein thrombosis and pulmonary embolism. Final results of the study are expected to be published shortly.

Meat-Eating Pacifists?

A recent report suggests that lowering your cholesterol levels may not be such a good idea after all. A meta-analysis of numerous studies has found a significant association between low or lowered blood cholesterol levels and violence, especially in men. Low cholesterol levels may reduce central serotonin activity, which is causally linked to violent behavior. Although the study does not rule out the influence of other environmental factors, the author recommends that the increased risk for violent outcomes should be included in risk-benefit analyses of cholesterol screening and treatment programs.

Source: Golomb (1998). Ann Intern Med. 128:478

Angiogenic Therapy For Coronary Artery Disease

Using recombinant fibroblast growth factor (FGF-1), researchers have succeeded in inducing new vessel growth in patients undergoing coronary artery bypass graft operations. In a randomized controlled trial, the angiogenic protein FGF-1 was injected into ischemic myocardium close to the left anterior descending artery and distal to its anastomosis with the internal mammary artery. Angiography performed 12 weeks later demonstrated coronary artery neovascularization extending out of the FGF-1 injection sites. In addition, stenoses distal to the anastomosis were bridged by new vessels. In contrast, patients injected with inactivated FGF-1 showed no evidence of myocardial neovascularization over the same period. Based on these exciting results, heart specialists may soon have another weapon in their fight against coronary artery disease.

Source: Schumacher et al. (1998). Circulation. 97:645.

Is Therapeutic Touch a Hoax?

Therapeutic touch (TT) practitioners claim to treat many medical conditions by using their hands to manipulate human energy fields. TT is based on the premise that people possess energy fields that are both detectable and modifiable. However, a new study casts serious doubt on the validity of TT. In the study, TT practitioners rested their hands (palms up) on a flat surface, and were asked whether they could detect the energy field of an unseen person who hovered his hand over one of the practitioner's hands. In the initial trial, the practitioners stated the correct location of the subject's hand 47% of the time. In a subsequent trial, practitioners were allowed to feel the subject's hands in advance and choose which hand the subject used for testing. The practitioners were then successful in only 41% of tries. As chance alone would predict an average score of 50%, the authors argue their results show that TT claims are groundless and that the further medical use of TT is unjustified.

Source: Rosa et al. (1998). JAMA. 279:1005.

New Drug for NIDDM

Non-insulin dependent diabetes mellitus (NIDDM) is characterized by insulin resistance, increased hepatic glucose synthesis and decreased pancreatic secretion of insulin. In NIDDM, peripheral insulin resistance precedes glucose intolerance in the majority of patients. Now, a large double-blind study has found that a new drug, troglitazone, reduces insulin resistance by sensitizing peripheral tissues to insulin action, thereby reducing the need for insulin. In the study, troglitazone was found to significantly decrease blood glucose levels and glycosylated hemoglobin values. Furthermore, combined troglitazone and metformin therapy led to even greater glycemic control. A notable side effect of troglitazone was the potential to cause hepatic dysfunction in 2% of patients. This new drug may now become first-line therapy for patients with mild NIDDM.
Source: Schwartz et al. (1998). N Engl J Med. 338:861.

Residents Report Mistreatment Rampant

An April 1998, study has revealed that residents perceive they are badly mistreated during their first post-graduate year. Steven Daugherty at Rush Memorial College in Chicago surveyed over 1277 second year residents and asked how they felt about their first year of residency. A stunning 93% of residents felt that they had been mistreated during their first year of residency. Public humiliation or belittlement was the type of mistreatment most often cited, and attending faculty and higher level residents were the most often cited perpetrators. In addition, 63% of female residents felt themselves to be victims of discrimination or sexual harassment. Overall, residents reported a moderate level of satisfaction with their residency with an average rating of 4.56 (good) on a scale of 1 (poor) to 7 (excellent).
Source: Daugherty et al. (1998). JAMA 279:1194.

Texas Team Touts Terrific Test

A newly developed assay may help physicians identify malignant tumours earlier than was previously possible. The new technique uses a laser to, "detect, enumerate, and characterize carcinoma cells in the blood." The test is exquisitely sensitive and can detect as little as one carcinoma cell in one milliliter of blood. The hope is that the test will identify shedding of malignant cells from primary tumours at a very early stage. The study also demonstrated a good correlation between clinical status and the number of tumour cells in the blood. The more advanced and invasive the disease, the more carcinoma cells were found. To date, the technique has only been examined for breast and prostate cancer. The present assay may be helpful in early detection, in monitoring disease, and in prognostication.
Source: Racila et al. (1998). PNAS 95:4589.

H. Pylori Falls Upon Hard Times

Helicobacter Pylori has enjoyed more than its fifteen minutes of fame since its identification as the pathogenic agent in many cases of peptic ulcer disease. It has been felt for some time that a weakly positive correlation exists between chronic gastric infection with *Helicobacter pylori* and coronary heart disease. If this association is causal, it was felt, then infection with *H. pylori* may increase the incidence of coronary heart disease by affecting other vascular risk factors. However, according to a recent meta-analysis published in the *British Medical Journal,* previous claims of a link between infection with *H. Pylori* and coronary heart disease were largely or wholly due to chance or to the preferential publication of positive results. The meta-analysis looked at 18 studies involving 10,000 people.
Source: Danesh et al. (1998). BMJ 316:1130.

The Truth About Creutzfeld-Jacob Disease

European investigators have recently completed a collaborative study of risk factors for Creutzfeld-Jacob Disease (CJD) in which genetic factors, medical history, occupational history, animal exposure, and diet were studied. The study revealed that there is little evidence for an association between the risk of CJD and either animal exposure, or consumption of processed bovine meat or milk products for the period studied. No significant increased risk of CJD in relation to a history of surgery or blood tranfusion was shown. There was no evidence for an association between the risk of CJD and the consumption of beef, veal, lamb, cheese, or milk. The study did however show an increased risk in relation to consumption of raw meat and brain and frequent exposure to leather products. The authors of the study warn that these results should be interpreted with great caution.
Source: van Duijn et al. (1998). Lancet 351:1081.

Triglycerides Linked to Heart Disease

It has long been known that by altering one's smoking status, blood cholesterol levels, blood pressure and physical activity, it is possible to also alter one's risk of myocardial infarction. It now appears that a new risk factor may be added to the list. A study published in *Circulation* found that high levels of blood triglycerides may exert their adverse effect by altering the size of low density lipoprotein (LDL) particles. Smaller, denser particles are more likely to promote atherosclerosis and subsequent myocardial infarction.
Source: Jeppesen et al. (1998). Circulation 97:1029.

Antenatal Care in Rural North India: Learning to Appreciate the Woman Beyond the Womb

Rachel Dayan (9T8)

An Introduction to India

As I embarked on my journey to India to complete a medical research project, I entertained romantic notions of exploring an exotic country at the periphery of the modern world. During my summer's stay, however, I came to realize that life in rural North India represents the way the majority of the world lives. Three quarters of the world's population lives in villages and 1/7 of the world's population lives in the 560,000 villages in India.[1] It is urban North America that is the anomaly.

Much of the fascination surrounding India is encapsulated in the simple statement that "India, of all lands, is one of extremes and paradoxes."[2] Consider its population. India is the second most populous country in the world with 960 million people and it supports 15% of the world's population with only 2.5% of the world's total land area.[3] Each year, the country grows by 15 million people which is equivalent to the entire continent of Australia. Some time in the next century, India is expected to surpass China as the most populated country in the world, but China's one billion people live in a territory three times the size of India.[1]

The paradoxes of life in India are best illustrated by the women. A woman's place in Indian society is fraught with contradictions. Although vast numbers of Indian women are illiterate, many hold important positions in politics and the arts. While many suffer discrimination and poverty, others are successfully transforming India into a modern nation which is the world's largest democracy. Despite producing some of the most powerful women in the world, such as Indira Ghandi, most village women are unaware of their rights.

The "typical" Indian woman lives a simple existence in a small, and often isolated village. This prototypical woman represents 75% of the 400 million women and female children living in India.[1] She almost invariably shoulders a triple workload which includes the multiple demands of productive work, household maintenance and childbearing and rearing. She must not only face interhousehold inequalities – such as the disparity between the rich and the poor, the discrepancies between high and low castes and the difference between rural and urban living, but she is almost undoubtedly a victim of intrahousehold gender inequality.[4] Whether in socio-economic indicators, such as education, health and work, or more subtle terms of power, decision-making and self esteem, the inferior position of most women in India has been consistently documented.[5]

The explanation for a woman's place in Indian society can be found in traditional Indian culture. India is a country where the birth of a female child is often viewed as a misfortune and where almost every woman has heard of the traditional blessing given at Hindu weddings, "may you be the mother of a hundred sons." The importance ascribed to a male child is evidenced in the country's female to male sex ratio of 930/1000, which is one of the lowest in the world. In most societies, females enjoy a biological advantage in survival compared with males. In India, every sixth infant death is believed to be due to the discriminatory treatment of female children.[5]

In fact, a woman's worth in Hindu culture is commensurate with the number of male children she has produced. The extreme value ascribed to a male child has both economic and religious origins. A son is considered social security for his parents. Not only will he receive a dowry from his wife at the time of their marriage, but he and his wife will continue to live with his parents to support them in their old age. At the funeral of his parents, a male child is required to perform cer-

tain rituals to ensure their direct path to heaven. After marriage, a male is not merely a husband or partner for his wife, but he is considered her provider, her protector and her god.

Another commonly cited indicator of the status of women in India is the rate of maternal mortality (MMR) which is considered to be among the highest in the world.[5] A direct indicator of reproductive health care,[6] the MMR in India is 500 deaths per 100,000 live births and even this is considered to be a conservative estimate.[4] Stated somewhat differently, a woman in India runs a 300 time greater risk of dying in pregnancy and childbirth than women in the developed world.[6] However, maternal mortality is believed to be the tip of the iceberg of reproductive problems. According to the WHO estimates, for every maternal death there are sixteen women who suffer morbidity that can persist throughout a woman's lifetime.[4]

With the knowledge that reproductive health problems are more common and are especially grave among the poor living in rural areas,[4] and fuelled by pervasive statements about the paucity of knowledge regarding woman's health, such as "information on health during the reproductive years is scanty and scattered"[4] and "most Indian data is drawn from hospital based studies and is not representative of the community," I set out to investigate the antenatal care available to women in rural Himachal Pradesh.

Life in Himachal Pradesh

The state of Himachal Pradesh (H.P.) is situated in the north of India, amidst the breathtaking Himalayan mountains. On its eastern side, H.P. forms India's border with Tibet. The state is generally mountainous, with altitudes ranging from 460-6400 metres above sea level. Although it occupies 1.69% of the India's total land area, it accounts for only 0.61% of the country's total population.[7] Geographically the state is divided into three zones: an outer Himalayan zone which is the most populated area of the state, an inner Himalayan region consisting of rugged mountains and narrow valleys with a lower density of population and a third zone of alpine pastures which remain snow covered for most of the year and are very sparsely populated.[8] Perhaps the most daunting aspect of nature that faces residents of H.P. is the severe monsoon rains. Parts of the outer Himalayan zone receive the second highest rainfall of anywhere in the world.

The state is the least urbanized of all Indian states, with only 7.6% of the population living in the urban areas compared with the national average of 23.31%.[8] Furthermore, 90% of the state's villages have populations that do not exceed 500 persons. Thus, the low density of small, highly scattered villages poses significant problems in the delivery of healthcare.[7] In fact, H.P. ranks last in the country in terms of villages served by primary health centres (staffed by physicians and "multi-purpose workers" [MPWs] who function as nurses) and primary health sub-centres (ambulatory centres staffed by MPWs alone). Each health subcentre in H.P. covers more than 9 villages, which is more than twice the national average and each primary health centre serves almost 74 villages.[9] Only 6.7% of villages have health centres within 2 km compared to the national average of 12%.[7] With inadequate governmental health service delivery in this area of the country, the importance of non-governmental organizations (NGOs) and their contribution to healthcare is immeasurable.

In H.P., the lowly status of women in India's predominantly patriarchal society is compounded by the isolation inflicted by the rugged terrain. Not only do women have relatively little access to healthcare or social supports or services, but the discriminatory cultural taboos persist because these rural inhabitants have relatively little exposure to outside influences. For instance, pollution taboos related to pregnancy and childbirth are a unique feature of hill cultures. Childbirth, considered a particularly dirty event, traditionally takes place in the cattleshed, where mother and child are confined for several days. Similarly, during menstruation, women are not allowed to cook or serve food, enter the temple or touch men. In fact, in some areas of the state, women are not allowed to enter the house at all during their menstrual cycle. Another particularly restrictive dictum maintains that any women attempting to break out of her cultural role is surely a witch to be punished through any available means. Finally, the value attached to the deliverance of a female child to her home of marriage while still virginal and "unpolluted" has led to the widespread state practice of marrying off girls between the ages of ten and fifteen. Despite the fact that the Child Marriage Restraint Act has been in place for four decades, making it illegal for females to be married under the age of 18, 40% of H.P. girls are married by the age of fifteen.[8]

Cultural beliefs aside, the life of a woman in H.P. is demanding and often quite punishing. She must bear the burden of a workload, that in all spheres, exceeds that which is shouldered by men. Studies have shown, that the total number of work days and the average number of hours of work per day for women in agricultural activities exceeds that of men. In fact, 75% of the agricultural work done in the state is done by women. In addition to her "productive work" requirements, Himachali women are essential for childbearing and rearing and are almost exclusively involved in the "unproductive" work of household maintenance. This domain includes the daily chores of food preparation, cleaning the house and fetching water; and the daily chores of collecting firewood, carrying dung from the fields to make dung cakes for fuel, washing clothes, grinding grain, and buying rations from the market.[8] Indeed, the endless cycle of drudgery facing the women of H.P. is a vivid illustration of world bank president Barber Conable's statement that "women do two thirds of the world's work . . . yet they earn only one tenth of the world's income and own less than 1% of the world's property. They are among the poorest of the world's poor."[1]

The Study and A Greater Understanding of Holistic Health Care

The lessons that I ultimately learned in India were somewhat different from those I initially set out to learn. I applied for and received funding from the International Health Program at the University of Toronto to assess the level of antenatal care provided to village women by Chinmaya Tapovan Trust (CTT), a non-governmental organization (NGO) run by a paediatrician in the state of Himachal Pradesh.

A comparative study was designed to determine the knowledge, attitudes, practices and skills of women with respect to three crucial aspects of antenatal care in developing countries: the need to receive two doses of tetanus toxoid to confer protection prior to delivery, the importance of iron and folate supplementation during pregnancy, and the recognition of danger signs indicating the need to seek further medical care. Using a questionnaire administered by a female interpreter, 42 women serviced by two of Chinmaya's health subcentres and 30 women serviced by two government health subcentres were interviewed. The government subcentres were matched to CTT centres based on geographical terrain, development of the villages and demographics of the population served.

The subcentres were carefully selected to represent the diversity of village life in H.P. Whereas some villages were on relatively flat terrain, others were ensconced in the mountainous Himalayan foothills. Although some villages had paved roads surrounding them, many could only be accessed on foot after descending into the depths of valleys, crossing churning rivers and then scaling rocky mountainsides. Despite the few villages that showed the beginnings of modernity with electricity, latrines and running water, most relied solely on dung cakes for fuel, promoted defecation in nearby fields and the collection of often contaminated water. The conditions of life in rural H.P. were amazingly disparate. Yet, there was one unifying factor across all villages that I encountered; the reliance of women on domiciliary visits by MPWs for the essentials of their antenatal care.

The Indian government has identified two measures which confer significant potential benefit on a pregnant woman and her fetus: the administration of tetanus toxoid immunizations and the distribution of iron and folic acid supplements. In India, neonatal tetanus is one of the major causes of death in the first four weeks after birth. In fact, in rural areas, 39.2% of neonatal deaths are due to tetanus.[7] Other studies in India have demonstrated that the MMR is five times higher and the stillbirth rate is up to six times higher in anemic women as compared to non-anemic women.[7] In rural Himachal Pradesh, where hookworm is endemic, the prevalence of anemia in women may be as high as 90%.[4] Therefore, standard practice in the care of antenatal women in rural India, by both governmental and non-governmental MPWs, includes tetanus toxoid injection if a woman is in her first pregnancy or if her last immunization was more than three years ago as well as the allocation of at least a three month supply of combined iron and folic acid supplements. Also, it is incumbent upon the MPW to provide regular check-ups in order to identify conditions which may require further medical intervention, as the main causes of maternal deaths in rural areas of the country are hemorrhage, anemia, abortion, toxemia and sepsis.[4] My goal was to interview pregnant women who were served by NGO MPWs and women who were served by government MPWs to determine how well the aforementioned objectives were being met.

As the study progressed, I slowly began to realize how inadequate my conception of optimal antenatal care actually was. To examine the workings of governmental and non-governmental organizations with respect to the stated antenatal care objectives could only have limited efficacy in the broader scheme of an Indian woman's life. According to the Indian government, 50-82% of the people in rural areas live below the poverty line and more than half of the rural population (approximately 260 million people) cannot even eat the minimum food necessary to survive.[7] Indeed, what is the use of iron-folic acid supplementation if basic nutrition is lacking? What is the utility of tetanus toxoid immunizations if knowledge about basic hygiene and sanitation is unknown? What is the utility of counselling about complications of pregnancy if the workings of a healthy female are not understood? These questions forced me to redirect my thinking to appreciate the importance of holistic care in the context of rural North India.

In fact, it is this appreciation of the whole woman that was the most salient difference between the antenatal care administered by CTT subcentres as compared to government subcentres. Upon analysis of the quantitative variables that my study was designed to enumerate, both CTT and the government MPWs gave similar numbers of immunizations and dispensed comparable amounts of iron and folic acid supplements. However, the CTT MPWs were true innovators in those aspects of holistic healthcare that were most difficult to measure. Their efforts far outstripped those of government MPWs. With one of the highest rates of maternal mortality in the world, the majority of Indian women's health programs are targeted to improve reproductive health. Despite the traditional view that maternal mortality is the major cause of death in Indian women, the literature shows that deaths due to pregnancy and puerperal causes account for only 11% of the total deaths which occur among women in India.[7] In fact, the greatest number of deaths in the female population occur before the age of 15 and not during the reproductive period.[7] In order to truly have impact on the high death rates and the low life expectancy among Indian females, it is imperative that economic, cultural, social and legal factors be evaluated and appropriately modified. Simply stated, the health problems of rural women are mainly related to their poverty and their inferior status in society.

CTT achievements in women's health stem from the recognition that poor reproductive health is a reflection of a series of different factors which go beyond the health sector and are not responsive to short term solutions. In order to implement lasting change, the CTT MPWs have a multitude of roles that surpass government antenatal care. The CTT MPW functions as an agent of change and an advocate for the people by actually living in one of the villages served by her subcentre, something that is not done by government MPWs. As an active participant in village life, she not only gains the trust of the villagers, but she spends a majority of her time in the village understanding and dealing with the root causes of illness, rather than merely treating people as they fall ill. Some of the work accomplished by the CTT MPWs during my summer in India included adolescent and women's groups which served as a forum for the discussion of health and hygiene, women's legal rights and methods of income generation; programs to plant trees, treat drinking water and properly dispose of garbage; and a daycare for young children whereby mothers

were able to do productive work while providing a stimulating environment for the child.

Perhaps most importantly, a CTT MPW strives to empower the women who have traditionally been marginalized within Indian society. CTT has recognized that lasting change in a society can only come about when people are encouraged to develop the confidence to solve independently their own problems. Consequently, the CTT MPW often works to facilitate the discovery of solutions to problems from the villagers themselves. The theme underlying all of CTT's work with women is that long term gains must not be sacrificed for immediate results. Thus, instead of merely dispensing vitamin and mineral supplements, the CTT MPW encourages villagers to devise ways to improve their overall level of nutrition. Instead of merely giving tetanus toxoid injections, the CTT MPWs work to improve a woman's personal hygiene and the village's overall sanitation. It is this appreciation for the broader determinants of health that make CTT's delivery of service quite exceptional and most inspirational.

Applicability of Lessons Learned in the East

Despite being immersed in a society so different from my own, India taught me several invaluable and practical lessons. My experiences in India led me to question my assumptions about the way that a society governs itself, the power of religion and cultural dictates in deciding the roles of men and women and the various determinants of health. Not only did I learn about a fascinating country, but I discovered a depth to my own culture that I never knew existed. But most compelling of all is how rural India highlighted the shortcomings of Western medicine. In an age where the potential of Western medicine to heal is unprecedented, patients have never been more disillusioned with medical practitioners. Despite vast technological accomplishment in medicine, more and more people are seeking alternative forms of healthcare. After seeing the emphasis that NGOs in India place on the economic, political, social and cultural aspects of illness, I truly believe that present levels of dissatisfaction with the medical profession may be attributed to our inability to recognize the varied components which give rise to the presentation of a medical problem. Indeed, Western medicine could do very well to take notice of health care delivery in its simplest, most unadulterated form, where it is the person beyond the patient that is appreciated.

Conclusion

I arrived in India believing that, with my study of antenatal care in rural North India, I could make a meaningful contribution to the society that welcomed me for a summer. At times it seemed that innumerable factors were conspiring to prevent the evolution (let alone the completion) of the study. The monsoon rains were often debilitating: communication and transportation were drastically reduced, getting to and travelling within villages required one to climb mountains and cross rivers on foot, and when homes were finally reached to conduct interviews, women were frequently out working in the fields. The setbacks that I endured during the course of the project seemed nearly maddening at times. However, as the haze of disappointment and apparent defeat gradually cleared, I began to see how much I had gained.

When I managed to step outside myself, I realized that the frustrations that I came up against during the implementation of a three month study were the same difficulties that consistently face the grassroots healthcare workers during their provision of service in rural North India. I developed a profound respect for those working towards a vision of improved health for Indian women despite an endless array of obstacles, both tangible and intangible. Throughout my summer, I cultivated a genuine appreciation for the many biopsychosocial determinants of health and I witnessed the extraordinary benefits that come from the application of preventive medicine. When I finally left India, I realized that rather than leave my mark on the country, its people left an indelible imprint on me, forever changing my feelings about true health and healthcare.

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Adult Hypotonia: A Case of Flaccid Physiology

Michael J. Angel, Ph.D (OTO)

The great neurologist Gordon O. Holmes claimed that a limb becomes more pendulous following a deep tendon reflex in patients with cerebellar lesions, than in healthy people. This was due to an apparent decrease in resting tone and was termed 'hypotonia.' Holmes believed that a healthy muscle at rest has a degree of tone, or activity, that resists passive movement. The concept of resting tone has become deeply ingrained in the teachings of many neurologists. Textbooks speak of this apparent resting tone in the healthy adult, as if it is a truism; as every cell has a sodium-potassium ATPase so too do all healthy striated muscles have a background of activity. Students readily accept this, as if it is something that seems to make general sense. Maybe it is reassuring to know that their muscles are working even when they aren't even trying. On the other hand, some thoughtful neurophysiologists say, "poppy-cock" and claim that hypotonia in the adult is the biggest load of bunk since the transient rise in Florida Everglades real estate. Is there any electrophysiological evidence for the existence of resting tone, or hypotonia in patients with lesions of the CNS? What is the mechanism of resting tone? Could it be that for so many years, so many medical students and residents have been sold so much snake oil? Evidence refutes the existence of adult hypotonia, but to this day educators of neurology, through blind faith and tainted texts talk about a reduction of normal resting tone following lesions to the CNS. And so many neurologists and neurosurgeons repeat what they have been taught, and what their predecessors have been taught, and so on, right back to when Holmes himself made his initial hypothesis.

Well, what does basic neurophysiology tell us? We know that in order for a muscle to exert a detectable force several necessary conditions must be met. First an action potential must be generated in a spinal motoneurone. This action potential exits the spinal cord, travels dutifully down the motor axon and terminates in motor endplates where it reliably induces suprathreshold activation and excitation-contraction coupling of several motor fibres. Muscles fibres respond by shortening. Active muscular force can only be generated if these conditions are met. With the use of surface recording electrodes, or needle recording electrodes on a person's arm or leg, an electrical correlate of this contraction can be recorded, i.e. an electromyogram. Electromyograms can easily record the activity of even a single motor unit. It is of significant interest to note that resting muscles do not generate any activity on the electromyogram. In other words, *resting muscles do not generate active force.* If resting muscles exert no force, how can there be a decrease in something that doesn't even exist? To this end the neurologist William Landau wrote, "The discovery by electromyography that normal relaxed striated muscle has no contractile activity has been an historical embarrassment."[1]

Lets go back to Holmes' original observation that has formed the basis of hypotonia. A hypotonic limb will be more pendulous following a stretch reflex i.e. the hypotonic limb will oscillate more than a healthy limb following tendon tap. Pickett and Tatum (1984), however showed that the leg pendulum test is not a sensitive measurement of lesions of central motor pathways, and that the only condition that lead to predictable, prolonged leg-swinging was Ehlers-Danlos syndrome, a disorder of collagen leading to lax joints and decreased visco-elastic forces.[2]

The obvious rebuttal is that although resting muscle may not have tone, activation of primary or secondary muscle afferents in response to passive motion may evoke motoneuronal activation which may generate force. It has been suggested that the mechanism for 'hypotonia' is the removal of a tonic stretch reflex.[3] Theoretically, this tonic stretch reflex would offer some resistance to passive move-

ment, and its removal would decrease this resistance. No systematic bedside examination of reflex activity had ever been performed on normal or 'hypotonic' patients, so this mechanism for hypotonia remained entirely speculative and had no supportive evidence. Van Der Meche and Van Gijn (1986) examined the electromyographic activity of normals, and patients diagnosed with 'hypotonia' using a number of slow and fast passive movements of their legs.[4] Patients' legs were released from the horizontal plane and allowed to drop freely, bending at the knee joint. Electromyograms of knee extensor and flexors were obtained during this fall and determined the presence of muscular activity. Fall-times were also obtained. Analysis of the timing and pattern of muscular activity could reveal if the activity was evoked through stretch reflexes or through voluntary control. Three questions were addressed, and are quoted directly below:

"1. Is there any EMG activity during passive stretch? If not, then the concept of hypotonia cannot be sustained.[4]

2. If activity is present, is it reflexive and does it contribute to the resistance felt? If this is so, hypotonia may be explained by decreased long-latency stretch reflexes.[4]

3. Does voluntary activity during passive movement contribute to the resistance? Voluntary activity during passive movement decreases with weakness and this could lead to an impression of diminished tone in conditions such as polyneuropathy and acute phases of paraplegia and hemiplegia."[4]

Electromyography indicated that almost all of the activity in the healthy and 'hypotonic' volunteers were in muscles which assisted the movement and were volitional in origin. Furthermore, the only difference in fall times (the time from horizontal orientation of the leg to vertical) were in a small number of healthy volunteers, who generated force through *voluntary* activation of the knee extensor muscles. It would be expected that if a resting, measurable tone existed in the quadriceps muscle, then 'hypotonic' limbs would have consistently shorter fall-times; this wasn't so. The reflex-evoked activity was rare in both groups and could *not* generate clinically detectable forces. The force generated by volitional activity, however, was clinically detectable. Thus the apparent reduction of force in 'hypotonic patients' is the result of a weakness in voluntary recruitment of motor units in the affected limb relative to the uninvolved limb. The supposed background resistance physicians think they are sensing in healthy patients is in fact produced by volitional muscular contraction. This is not "resting tone."

Van Der Meche and Van Gijn conclude:

"During passive movement of a limb, voluntary activity is present in most control subjects and is responsible for most of the resistance. This activity bears no relation to any definition of tone either in a physiological or in a clinical sense. Therefore the term "normal tone" is not appropriate and should be abandoned. 'Hypotonia' originates from the same erroneous concept; flaccidity as a result of weakness is a better term, and is already used in the literature. Passive movements during the clinical examination are still of great value, but only to detect spasticity or rigidity."[4]

I challenge students to put a stop to the erroneous teachings of adult hypotonia. It is muddling the minds medical students who know not the workings of the spinal cord nor the minutia of muscle spindle afferent physiology! On a practical (and less inflammatory) note, when performing the exam of the motor system practice relaxing your patients. Ensure they are fully supine when testing for abnormal increases in tone. All joints proximal to the one being tested should not bear weight; this will help them relax. Take your time; tone cannot me measured hastily. Finally, and most importantly, remember that yelling at your patient to relax their wrists or elbows will not work in your favour.

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The Medical Research Council of Canada: Where is Canada Headed?

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Research is the cornerstone of the medical profession and Canada has traditionally been a leader in this field. Last year, Canadian researchers ranked number one in the world in efficiency and impact of publications per dollar invested in research and development.[1] In order for medical research to occur in any field, in addition to the expertise of the researchers themselves, it requires a large financial commitment. Medical research in particular has tremendous financial requirements. The Medical Research Council of Canada (MRC) is the major federal agency responsible for the funding of health research and training in Canada and has been in existence since 1960.[2] The MRC of Canada operates on a granting basis; grants typically last from one to five years, depending on the perceived need of the proposed project. In order to receive a grant, a research project proposal must be formally submitted and selected by the MRC peer-review committee. The grant system is in keeping with the mandate of the MRC, which is "...to promote, assist, and undertake basic, applied, and clinical research in the health sciences at an internationally competitive level."[3] The money, which is received by the MRC predominantly through federal funds, is used not only to support individual projects, but also to cover equipment costs of current researchers as well as the training of future scientists.

Last year (1996/97) the MRC budget was $242 million dollars; however, since 1994 the budget has been reduced by 13%. This is in stark contrast to other G-7 nations whose governments have been steadily increasing financial support over the past few years.[4] Canada is in danger of both losing its status amongst the G-7 in research, and being unable to fulfill the MRC's mandate. The importance of health research in Canada, how research funding is changing in today's economy, as well as how the MRC and the University of Toronto interact are all important issues to be aware of both as medical students and potential future researchers.

Why is research so important and why does it deserve funding? These are important questions that must be answered in order to gain the perspective needed to properly assess Canada's situation. Basic and clinical research have both economic and social benefits. On a fundamental level, research contributes to a healthier society through innovation, improved treatments and diagnosis. It enhances the scientific knowledge base and is the backbone of evidence based medicine, which has become the norm in Canada. Equally important, although often overlooked, are the economic gains generated by research. MRC operating grants create highly educated job opportunities, and generate exportation opportunities of both ideas and the products that result. They can lead to new company development and spin-offs, the primary example being the recent growth of the biotech industry in Canada. These factors lead to economic growth and an increased standard of living for all Canadians. It is unacceptable for Canada to take a passive position and let other countries such as the United States take away these opportunities and do research for us.

In order to maintain the quality of research that has come to be expected in Canada, financial support must be gained. Canada is spending less money while other countries such as the United States, United Kingdom and France are increasing their budgets for health research.[4] A key feature of the research economy is its mobility. It is common for successful Canadian researchers to move to

other countries, where they will receive the funding they need to survive. Last year in Canada, only one in five grant applications were approved for funding, and of those that were funded many were given less money than in the past.[5] Thus, not only is Canada losing the top researchers of today, but it is also losing many potential researchers. According to the MRC, one way to address these concerns lies in the private sector. As public funding dwindles, private corporations in the health research field are being relied upon to fill the void. This shift is evident today in funds such as the *Burroughs Wellcome Fund,* which contributes over $1 million to the MRC that ultimately goes to funding all areas including a portion of summer research scholarships given to medical students.[3] The Pharmaceutical Manufacturers' Association of Canada (PMAC) has invested more than $115 million in personnel and research projects via the MRC.[3]

One of the main concerns arising from the issue of private funding is the potential to lose objectivity when allocating grants. Canada no longer has the luxury of an entirely public and self-contained research program. Will scientists lose control over their work? Will private companies choose research based on personal interests of shareholders rather than the interest of humanity? The answer to both questions is no. The MRC will continue to operate via a peer-review committee, which is selected by the MRC and not the private sector. It is this committee that allocates research grants and funds. Clearly, the private biotech and pharmaceutical industry has an interest in the continuation of research and is not simply donating the money without considering its own financial responsibility to its shareholders. In order for these Canadian companies to continue to grow, research must generate the products and innovations of the future. So both medical research and the Canadian biotech and medical industry stand to benefit greatly from this mutual relationship, as they have already begun to do.

These changes will benefit research centres across Canada, including scientists at the University of Toronto, many of whom have received long-standing support by the MRC. Toronto is the fourth-largest health research centre in North America. In the past year, the University of Toronto received over $42 million, which went towards 468 operating grants, 67 salary-supported investigators and 401 research trainees.[6] All of Toronto's major research centres such as the Hospital for Sick Children, Mount Sinai Hospital, The Baycrest Centre for Geriatric Care and the Clark Institute of Psychiatry depend on this funding to continue to conduct research by the high standards that they have been accustomed to. Despite these numbers, researchers in Toronto had only 53 new grant applications approved out of 213 submitted proposals for the most recent grant competition in September of 1997. This success rate of roughly 25% is only slightly higher than the nationwide average of 20%.[5] Some of the Toronto researchers that have been successful with their project proposals include: Dr. Peter St. George-Hyslop, who has been working on genetic links to Alzheimer's Disease; Dr. Anne Bassett, who is investigating the genetics of schizophrenia; and Dr. Dan Drucker, who has discovered a naturally occurring peptide capable of stimulating growth of the small intestine lining, which is vital to nutrient digestion. Toronto and the rest of Canada is not short of new and exciting research ideas that can help solidify Canada's reputation as one of the world's best in scientific advancement. It would be a shame if these ideas cannot be given the time and resources they deserve because of financial shortages.

The future however is a bright one. The Canadian government has re-dedicated itself to research and development, specifically in the medical research area. Dr. Henry Friesen, president of the MRC, has adapted well to the new economic environment by securing new private sector dollars in addition to lobbying for federal funds. These efforts have resulted in the funding base for the MRC being increased by $40 million for the upcoming fiscal year (1998-99).[7] This money has already made its way to research institutes and universities across Canada. It is estimated that the grant application success rate will rise from 20% to 29%.[7] This new commitment of federal funds paired with new private revenue resources will hopefully assure Canada's place amongst the research elite.

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Ambiguous Policy and Student Apathy: A Dangerous Combination

Allan Kevin Grill, BSc. (OTO)

I was motivated to write this article as a reaction to student apathy. Medical students do not seem to care about some issues pertinent to our future and the future of our school. It is my hope that this essay will be a reminder of the potential influence we have in shaping school policy. First I will explain why a recent attempt to change the grading policy of the undergraduate medical program was unsuccessful, then I will emphasize the students' responsibility to make sure the next attempt is successful.

This past October, the University of Toronto Faculty Council of the Faculty of Medicine assembled to determine if there should be a change in the way students' grades are reported. This would apply to both the pre-clerkship (years 1 and 2) and clerkship (years 3 and 4) phases of the curriculum. Proponents of this proposal favour a new system in which marks are recorded as P (pass), F (fail), or D (distinction). Opponents of the proposal still believe in the traditional A, B, C or F. As an observer, the cacophony of consonants and vowels sounded more like a game of *"Wheel of Fortune"* than an academic debate. Ultimately, the motion was defeated by one vote. Yet the elation which accompanies an electoral victory was replaced by a feeling of uneasiness at the narrow decision. Usually, a motion that makes its way through the administrative process to be presented at Faculty Council gets passed with a substantial majority of votes. Why the split decision in this case?

Each side of the grading issue was equally championed and challenged. This made the choice very difficult. Although I was a leading supporter of the current letter grading system, I agree that it is far from flawless. The current system highlights a difference between a grade of 79% (B) and 80% (A). It seems that with such a narrow margin, there is not a significant difference in academic performance. Conversely, each student who receives an overall average of 80% or higher is indistinguishable from one another after receiving a letter grade of A denoting class honours. This is a very non-specific method to measure academic excellence, especially since over 50% of each class falls into this category. With the proposed motion, however, only the top 10% of students in each course would be distinguished for academic performance. This is an appropriate grading change because it is a less arbitrary method of awarding the high scholastic achievers.

What prevented the P/F/D motion from going through? For starters, it was confusing. Students were puzzled about the difference between an *official transcript* and an *official statement* of marks. The term *official transcript* is used to describe the grades that are entered into the computer by the Faculty of Medicine, while an *official statement* refers to the report card that each student receives at the end of each academic year. In the current grading system, these two terms are synonymous. Both record a student's numerical grades and corresponding letter grades (i.e. 80% = "A"). With the proposed grading change, however, the *official transcript* would record grades in a different fashion than the *official statement.* The *official transcript,* produced by the Faculty of Medicine, would start recording students' grades as P/F/D consistent with their new grading system. The official statement, produced by the University of Toronto, would continue to record numerical and corresponding letter grades consistent with the current grading system that includes the rest of the university faculties. This is due to the fact that the way marks are recorded on *official statements* can only be changed if there is an overall agreement by the faculties at the University of Toronto (U of T).

This confusing difference between the *official transcript* and *official statement,* created by the proposed grading motion in question, would significantly change the residency program application process. When the time to apply for a residency position arrives during fourth year, U of T is responsible for the academic portion of the application. The medical education office sends each student's *official transcript* to the appropriate schools. Although the current grading system enables the program directors to know the precise numerical grades of each U of T student, the proposed grading system would only report grades as P/F/D. As mentioned earlier, only the students falling within the top 10% of each course (a grade of "D" or distinction) would be recognized as achieving academic excellence. Despite the argument for a less arbitrary method of determining scholastic achievement, certain students would feel at a disadvantage in the new P/F/D system. For example, if a student received an 85% in a course, but did not fall within the top 10% of the class, they

would receive a grade of "P". They would be recognized by the residency program directors as being at the same academic level as a student who received a grade as low as 60%. Although this student did not receive a grade of "Distinction", it would be in their best interest for the program directors to see that they received a high grade of 85% as opposed to a low grade of 60%. Since *official statements* still record number grades in spite of the proposed P/F/D system, this student can exercise the option of sending a copy on his/her own to the appropriate schools that is separate from their U of T application.

This seems to contradict the whole purpose of the P/F/D motion twofold; it creates a system which simply panders to both sides, and it fails to eliminate student competition on the basis of minute discrepancies between grades. The latter point also weakened the motion's "national" perspective. It was argued that U of T should join the trend of Canadian medical schools (11 of 16) by adopting a P/F/D grading system. However, several of these schools (i.e. University of Manitoba, University of Western Ontario, McGill University, and Memorial University) also allow their students to request an *official statement* reporting their numerical grades.

The advantages of a P/F/D system also are questionable. Currently, only 33% of chairs of Canadian residency programs prefer receiving grades of this sort. In addition, there may be an increase in a student's stress level when trying to attain a grade of "Distinction" because one has to score within the top 10% of each course. Other students who find it difficult to reach such academic heights may develop a lack of motivation since they only need a 60% to pass. In fact, the Faculty of Medicine at the University of British Columbia recently changed the grading policy of its pre-clerkship clinical course for this purpose. In a telephone conversation, a fellow colleague reported that it was felt students were performing at levels below their potential despite adequate teaching. Now that the students are being evaluated via letter grades, the course is being recognized by students as having equal priority.

There are, of course, many counter arguments to the above statements. Currently, the Problem Based Learning (PBL) component of our curriculum has proven that students do work cooperatively and excel under a P/F system. It has also been suggested that there will be less pressure on students when it comes to studying for exams as they would only need 60% to receive a grade of "P". Students could spend more time focusing on areas of the curriculum which spark their interest.

It should be evident at this point that the issue of a grading policy is subject to endless debate, and we currently find ourselves at a stalemate. This is not, however, the first time that the Faculty of Medicine has been faced with this dilemma. Historically, U of T has been fickle with respect to this grading issue. The Faculty of Medicine during the 1970s changed their grading to P/F, but the following decade saw their colleagues revert back to our current system. Ironically, the main reason for both of these changes was to reduce stress among medical students. The important fact, however, is that both of these changes were initiated by students alone. Now in the 1990s, history has repeated itself via the grading policy debate. The major difference here was that medical students chose not to be involved.

Most of the discussion surrounding the grading issue was generated by members of faculty. Strange as it may seem, very few students gave their opinion. Even though this issue had been formulated by the Undergraduate Medical Education Curriculum Committee over a year ago, only 10% of the student body participated in a mock referendum prior to the Faculty Council meeting. The lack of student attendance also caused some controversy. Only 11 of the 23 medical student caucus exercised their right to vote. Of the 4 students who sit on the Medical Education Committee, which was instrumental in sending the motion to Faculty Council, only 2 were present. Their presence, incidentally, could have reversed the decision since a majority is based on a 50+1% format.

The student apathy in school politics is not unusual. For example, the U of T student governing body, also known as the Student Administrative Council, holds annual elections, but only 7% of the thirty-thousand undergraduate and graduate students exercise their right to vote (Smith, personal communication). The consequence of not voting manifests itself during the term of the elected student representative. Although they did not receive votes from the vast majority of students, the council position brings with it the power to be the representative voice of all students. It is frightening to realize how fast their policies can be passed when there are few people to oppose it, let alone discuss it. What is even more frustrating is when people reveal their opinion only after a motion has been passed. Most of the time their comments are worthy and may have had a significant impact on the subject of school policy. But by the time they make their ideas known, it is too late.

There are only a certain number of steps that can be taken short of forcing students to take an active role. Dr. Frecker, Associate Dean of Undergraduate Medical Education, makes certain everyone has access to e-mail. Faculty Council meetings are open to non-members, and the meetings' minutes are published each month for those who cannot attend. Our very own student government, the Medical Society, takes the responsibility of being aware of school issues. They make endless announcements during class time, and each member is more than happy to relay information if approached. Of course it is understood that medical students have many priorities. They have a heavy workload, and there are many extracurricular activities in which to take part. The issue of academic policy, however, cannot be ignored. A curriculum may remain static without proper feedback from students. Students bring new ideas and strengthen the relationship between themselves and the faculty. To further the incentive, remember that we are the future of academic medicine, and one day we will be formulating educational policies at the university level. A little practical experience will not hurt.

The issue of creating a new grading system is far from being resolved. Although this latest motion failed, there is a substantial number of faculty members who strongly support a pass-fail-distinction system. It is only a matter of time before another motion will be presented at faculty council. Since such a change solely affects the medical students at U of T, it is essential that more of their voices are heard before any decisions are made. Although the faculty has the students' best interests in mind, there must be direct communication to verify that these interests are shared. Since grading is a significant portion of a medical student's evaluation, they will benefit the most if they feel the marks fairly represent academic performance. Whether they prefer to be graded with A/B/C/F or P/F/D remains to be seen. The most important factor, however, is choosing a grading system they can be comfortable with, in order to finally receive the letters that really count - M and D.

Caffeine: The Good, The Bad, and The Ugly

Allan Eckhaus (0T0)

At a time when increasing patient education is being stressed, it is rather odd that among prevalent topics such as smoking, alcohol, and recreational drug use, the topic of caffeine has slipped through the cracks. For many, caffeine is a wonder drug – a means to get through long and demanding days. To others, it is just a wonder – a wonder how caffeine seems to have an effect on everyone but themselves, a wonder as to why so many university students have a coffee mug hanging from the back of their knapsack, and a wonder why coffee is not on the list of differential diagnoses for halitosis.

To dispel any myths concerning caffeine content in beverages – here are the facts:[1]

roasted and ground coffee	85 mg/250 mL
instant coffee	60 mg/250 mL
cola beverage	40 mg/300 mL
instant tea	30 mg/250 mL
decaffeinated coffee	3 mg/250 mL

It has been shown that dietary caffeine intake is consumed almost entirely in beverages.[1] The latest data indicates that two-thirds of the Western population consumes over 250 mg of caffeine per day, with coffee representing 90% of the intake. Estimates from the same study indicate that 20-30% of adult Americans consume more than 500 mg of caffeine per day.[2,4]

Caffeine acts as a diuretic, cardiac muscle stimulant, central nervous system stimulant, smooth muscle relaxant, stimulant for gastric acid secretion, and acts to elevate plasma free fatty acids and glucose.[1] On a more cerebral note, caffeine has been shown to antagonize alpha-1 and alpha-2 adenosinergic receptors in the limbic, hippocampal, and striatal areas of the brain. Adenosine is an endogenous substance that produces certain effects including sedation, bradycardia, and decreased blood pressure.[3] In essence, caffeine increases anxiety and consumption at high doses can mimic anxiety attacks. It also increases energy metabolism throughout the brain, while simultaneously decreasing cerebral blood flow.[4] As well, caffeine activates noradrenergic neurons and appears to influence the local release of dopamine and affect its action on serotonergic neurons.[4]

Aside from caffeine's anxiogenic properties, anecdotal and controlled reports suggest that the so-called "caffeine withdrawal syndrome" is both frequent and underdiagnosed.[6] One double-blind study reported an increase in depressed mood, anxiety, low vigour, fatigue, and severe headaches in subjects during the withdrawal period.[6] Withdrawal can occur in individuals that drink as few as two cups of coffee per day and in those that abruptly stop or reduce caffeine intake.[4] Furthermore, this effect can occur after only two weeks of coffee consumption.[4] This scenario is not unfamiliar to students around exam periods who do not drink coffee regularly, but begin consuming caffeine to stay awake.

A recent study on dogs has investigated the link between caffeine and cardiac arrhythmias. The data indicates that even at low doses, caffeine generates significant sinus arrhythmia, atrial tachycardia, atrial ectopic beats, wandering of pacemaker, and premature ventricular contractions.[5] Although this may explain certain coffee makers' new frequent buyer cards, entitling a customer who buys twelve cups of coffee to receive a week's worth of digoxin free, the potential for generating a caffeine-induced cardiac arrhythmia should be discussed with patients.

Furthermore, the DSM-IV has added acute stress disorder (ASD) as a new category to describe acute reactions to extreme stress. Combat-stress reaction (CSR) is a sub-category of ASD, occurring during war settings.[4] It has been proposed that caffeine, through its consumption and withdrawal effects can potentiate CSR.[4] I do not wish to imply that patient literature on combat-stress reaction be widely distributed. However, I would not be surprised to see a new coffee maker emerge under the name Nabomb, selling their version of the "scud-cinno" with and without froth.

It would be interesting to envision society's opinion of caffeine if it were only available as a pill or through intravenous injection. Would we be as accepting or as complacent as we are when caffeine is hidden in our drinks? Caffeine is a drug. Comparable to other drugs, it has its benefits and side effects. While coffee can be helpful in staying awake and alert, caffeine can increase anxiety, stimulate gastric acid secretion, and potentially generate cardiac arrhythmias. Patients deserve to be educated about caffeine's negative effects, so that they may make an informed choice the next time they desire a tasty hot beverage.

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More Than Just a Cold Sore

Denise Campbell, Ph.D (OTO) and
Jonathan Grynspan, BSc. (OTO)

Case Presentation

A 68 year old, right-handed retired female office worker was admitted to the hospital following a five day history of an acute febrile illness with focal neurological deficits.

Five days prior to admission the patient suddenly developed weakness in the first three digits of her left hand, left-sided facial droop, and slurred speech. The clinical presentation included fever, severe bitemporal headache, nausea, vomiting, chills, sweats, dizziness, and lethargy. There were no falls, vertigo, visual disturbances, or loss of consciousness. The patient experienced increased urinary frequency and urgency with no dysuria or hematuria. Three days prior to admission, the patient presented to the emergency room with the above symptoms. She was treated with Septra for a urinary tract infection and referred to a stroke prevention clinic.

During the ensuing three days the patient experienced increasing difficulty with articulation, slowing of speech, and excessive drooling. There was dysphagia with no distinction between solids and liquids. The bitemporal headache and drowsiness persisted, although the fever, nausea and vomiting resolved. On the third day she was admitted to hospital.

Significant past medical history included a six year history of rheumatoid arthritis which was being treated with methotrexate and ibuprofen. The patient had a 30 pack-year smoking history, and she had quit smoking 10 years ago. There was no history of alcohol abuse, illicit drug use or seizures. The patient's cardiac risk factors include being post-menopausal, and a significant family history for coronary artery disease. There was a family history of cerebral aneurysm. There were second degree relatives with multiple sclerosis (MS).

At the time of admission her medications included folate, ibuprofen, methotrexate, and Septra. Her admission vital signs were: temperature 37.4°C, pulse rate 76 and regular, respiration rate 16, and blood pressure 136/84 mmHg.

On examination, the patient was drowsy and excessively drooling, but she was in no apparent distress. She was alert and oriented to person, place and time. The neck was supple. There was decreased sensation to light touch and pain in the left V3 distribution. There was weakness on the left side of the face involving the forehead. The gag reflex was diminished. The remaining cranial nerves were intact. Tone in the left arm was slightly increased. Strength was 5/5 in all limbs. Pronator drift of the left arm was noted. The finger to nose test revealed dysmetria on the left side. The left heel to shin test was abnormal. Her gait was ataxic and wide based, and she could not perform tandem gait. Sensation to light touch and to pain was slightly diminished in the left arm. Extinction and agraphesthesia were noted on the left side. Two point discrimination was reduced on the left side. The deep-tendon reflexes were 2+ throughout, and the grasp and snout reflexes were present. The remainder of the physical exam was unremarkable.

The blood chemical and hematological values are shown in Tables 1 and 2. Blood cultures were negative. A chest X-ray and a CT scan of the head performed at the time of admission were considered normal.

On the second day in hospital the patient had a fever of 39.5°C accompanied by a decreasing level of consciousness and mild dyspnea. The neck remained supple. Urine and blood cultures were negative.

The patient's condition deteriorated on the third day in hospital as her level of consciousness continued to decrease, and she remained febrile with temperature spikes as high as 39.2°C. The patient became verbally non-responsive and minimally responsive to commands. She remained responsive to pain. Plantar response was now extensor bilaterally. Blood and urine cultures remained negative. A repeat chest X-ray showed no focal consolidation. Two attempts at lumbar puncture were unsuccessful. The patient was placed on ceftriaxone, ampicillin, and acyclovir. The family informed the team that the patient was congenitally asplenic. There was no previous history of abdominal surgery. A repeat CT scan of the head showed loss of the right insular ribbon, hypoattenuation posterior to the right sylvian fissure, and sulcal effacement.

On the fourth hospital day a fluoroscopic-guided LP was performed. The results are summarized in Table 3. Cerebrospinal fluid (CSF) cultures for bacteria were negative. CSF fungal cultures, India ink test, as well as cryptococcal and mycoplasma serology were negative.

Table 1
Hematological Laboratory Values

Variable	Value	Range
Hemoglobin (g/L)	139	120-160
ESR (mm/hr)	29	0-20
White-cell count (10^9/L)	8.7	4.0-11.0
Platelet count (10^9/L)	392	140-450
Neutrophils (10^9/L)	4.4	2.5-7.5
Lymphocytes (10^9/L)	3.1	1.0-4.0
Monocytes (10^9/L)	1.0	0-1.0
Eosinophils (10^9/L)	0	0-0.7
Basophils (10^9/L)	<0.3	0-0.3
PTT (sec)	25.4	26-38
INR (sec)	1.01	0.81-1.20
Complement – C3 (g/L)	1.5	0.7-1.8
Complement – C4 (g/L)	0.3	0.1-0.5
ANA	Positive (1:40 dilution)	Weak; homogeneous staining pattern

abnormal values are in italics in all tables

Table 2
Blood Chemical Values

Variable	Value	Range
Sodium (mmol/L)	132	136-146
Potassium (mmol/L)	4.2	3.6-4.9
Chloride (mmol/L)	96	100-109
Glucose (mmol/L)	5.4	3.2-6.4
Urea (mmol/L)	6.2	2.7-7.5
Creatinine (µmol/L)	116	<133
Liver Function Tests (LFTs)	Within normal range	

Table 3
Lumbar Puncture Values

Glucose (mmol/L)	3.9
Protein (mg/L)	*586*
Red cells (µ/L)	2
White cells (µ/L)	*230*
Neutrophils (µ/L)	0
Lymphocytes (µ/L)	*225*
Monocytes (µ/L)	5

An acute decrease in the patient's level of consciousness occurred on the fifth day post-admission. She became apneic requiring ventilatory support, and was transferred to the critical care unit in an obtunded state with a Glasgow coma scale (GCS) score of 8/15 (E-3, V-1, M-4 bilaterally). Medical imaging studies using magnetic resonance imaging (MRI) were performed. On the sixth day in hospital the results of a diagnostic procedure became available. On the seventh day her serum sodium was decreased to 123 mmol/L. Other lab values were not significantly altered.

CPC Discussion

Let us review the results of the medical imaging studies.

Dr. Richard Farb: CT scans of the brain performed at the time of admission to hospital demonstrated no abnormality. The CT scans were repeated on the third day in hospital. They showed hypodensity of the posterior aspect of the right insular ribbon (Figure 1a), and effacement of the sulci over the right frontal convexity (Figure 1c). On the CT scans performed nine days later, these abnormalities were more readily demonstrated (Figures 1b, d).

Figures 1e, f, g, h, and i are axial MR images performed on the fifth day after admission. Figures 1e, f, and g show the abnormality in the right insular cortex and subinsular white matter. Figure 1e is a T1-weighted and gadolinium-enhanced axial image showing mild enhancement of the right insular cortex. The enhancement in this area is shown in Figures 1f and g (a T2-weighted axial image and a proton density image, respectively). The effacement of the sulci over the right frontal convexity (Figures 1c and d) is demonstrated on the protein density MR image in Figure 1h.

The third and final radiological abnormality detected in these studies is shown in Figure 1i. This axial MR image (proton density) was taken more superiorly. It shows bilateral, parasagittal involvement of the cortex over the cingulate gyrus.

Impression: These abnormalities are consistent with the appearance of early infarcts or encephalitis.

Differential Diagnosis

The acute presentation of a febrile illness with headaches, decreasing level of consciousness, and focal neurological deficits is consistent with vasculitis, a cerebrovascular accident, or encephalitis.

Vasculitic syndromes can be classified as systemic necrotizing vasculitis (including polyarteritis nodosa), hypersensitivity vasculitis (exogenous or endogenous stimuli), Wegener's granulomatosis, giant cell arteritis, and other vasculitic syndromes.[1] The common denominator of vasculitic syndromes is the ischemic changes in the tissues supplied by the involved vessels.[1] This woman did not present with any skin manifestations of systemic vasculitis, nor was there any evidence of end organ ischemic damage consistent with a vasculitis. Vasculitis is a secondary manifestation of a primary disorder like systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and Sjögren's syndrome.[1] The patient did have a six year history of RA which was under control and she had not experienced any recent exacerbations. She was not on any new medications that would predispose to a hypersensitivity vasculitis. She had been taking methotrexate and ibuprofen without difficulty. In addition, she did not test positive for the presence of high levels of antinuclear antibodies (ANA). The complement levels were normal.

Rheumatoid vasculitis occurs in patients who are severely affected with RA and who have high titres of circulating rheumatoid factor.[2] It can affect nearly any organ system. Widespread systemic vasculitis and its sequelae are rare. Rheumatoid vasculitis usually presents in a limited fashion involving one organ system (e.g. mild distal sensory neuropathy or mononeuritis multiplex).[2] Neither of these conditions related to rheumatoid vasculitis affecting the nervous system has any relation to the case at hand.

Isolated vasculitis of the CNS is uncommon. This diagnosis

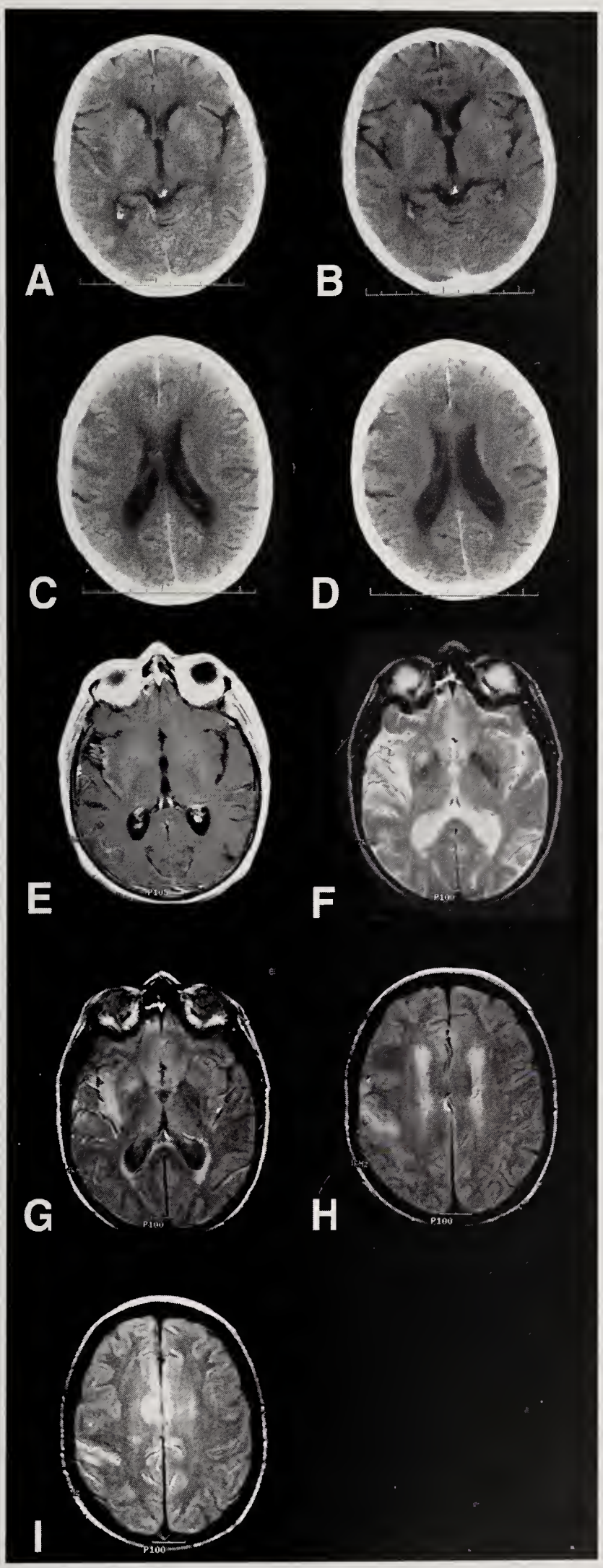

FIGURE 1.
Figures 1a and 1c. CT Scans performed on third day in hospital.
Figures 1b and 1d. CT Scans performed on ninth day.
Figures 1e, 1f, 1g, 1h, and 1i. Axial MR imaging performed on fifth day.

would only be entertained in this patient if the other more likely diagnoses were disproved. The diagnosis is made by arteriography to demonstrate characteristic vascular abnormalities, and confirmation is by brain biopsy.[1]

Five days prior to admission, this patient presented with an acute febrile illness. She had left-sided focal neurological findings and slurred speech in the absence of falls, vertigo, visual disturbances, loss of consciousness or behavioural changes. Her speech and left hand numbness improved over the next few days. This clinical picture is not consistent with a cerebrovascular infarct. In addition, she did not have predisposing risk factors for CVA such as arrhythmias, carotid atherosclerosis or hypertension. The normal CT scan at the time of admission, five days after the onset of neurological symptoms, suggests against infarction.

An acute clinical presentation that includes fever, meningismus, and headache raises the spectre of a central nervous system (CNS) infection. In a patient with an unexplained change in mental status and evidence of focal or diffuse neurological signs and symptoms, even without meningismus or fever, encephalitis must be considered.[4,5] A high index of clinical suspicion for encephalitis is necessary because it is associated with high morbidity and mortality. As well, the clinical outcome is often influenced by the speed at which treatment is started.[5]

It is important to rule out non-viral causes of encephalitis, both infectious and non-infectious. Table 4 provides a list of diseases which mimic herpes encephalitis as determined by the NIAID study of that disease.[6] Medical imaging studies will resolve abscesses, subdural empyemas, tumours, and subdural hematomas. It is necessary to obtain CSF for culture and sensitivity studies to detect bacteria, fungi, and viruses; particularly as it may take time for an abscess to form. Mycoplasma is not easily cultured, and tuberculosis cultures take six to eight weeks. Rickettsial and toxoplasmosis infections are detected by histopathology. This woman may have been mildly immunocompromised from her methotrexate use. Immunocompromised individuals are at increased risk of encephalitis from bacterial infections. HSV encephalitis can cause brain infection in both immunocompromised and immunocompetent individuals.

Vast arrays of different focal neurological findings of viral encephalitis have been reported. Different viruses produce different characteristic patterns of CNS injury, but it is impossible to distinguish the type of viral encephalitis based on clinical criteria alone.[4] While the pattern of brain involvement seen in imaging studies may be suggestive of different causes of encephalitis, the findings do not suggest an etiology with great sensitivity or specificity.[7] Indeed, according to the radiologist, without a clinical history, the radiological findings in this case would point toward ischemic injury.

It is important to elicit a travel history from a patient presenting with signs of encephalitis. Arbovirus infections cause 10% of all cases of sporadic encephalitis, and up to 50% in years with epidemics. These infections are spread to humans by mosquitoes and ticks.[8] These infections typically occur in epidemics during the summer months.[4] The midwestern and eastern United States have most cases of California encephalitis, and 90% of symptomatic cases occur in children. St. Louis encephalitis occurs throughout the United States, with children and the elderly most

prone to clinical disease. Western equine encephalitis commonly occurs in the western United States and Canada and is most severe in infants and young children. Eastern equine encephalitis is most common in the Atlantic and Gulf coast regions. Fortunately, this is a rare infection as it is the most severe of the arboviral encephalitides with a mortality rate approaching 70%.[8] In this case, the travel history was negative, and the encephalitis occurred in late autumn.

Table 4
Conditions which Mimic Herpes Encephalitis

Treatable Conditions	Non-treatable Conditions
Infections	Nonviral
Abscess/ subdural empyema	Vascular Disease
Bacterial	Toxic encephalopathy
Streptococcus viridans	Reye's syndrome
Bacteriodes melaninogenicus	Viral
Klebsiella pneumoniae	*** Togavirus infections:
Listeria	St Louis encephalitis
Fungal	Western equine encephalitis
Mucomycosis	California encephalitis
Cryptococcus neoformans	Eastern equine encephalitis
Rhizopodifirmis	** Other herpesviruses:
Mycoplasma	Epstein-Barr virus
Tuberculosis	Cytomegalovirus
Cryptococcal	Others
Rickettsial	***Echovirus
Toxoplasmosis	* Influenza A
Mucomycosis	***Mumps
Meningococcal meningitis	* Adenovirus
Tumour	Progressive multifocal
	Leukoencephalopathy
Subdural hematoma	* Lymphocytic choriomeningitis
Systemic lupus erythematosus	Subacute sclerosing panencephalitis
Adrenal leukodystrophy	

*** = common viral causes of encephalitis (including HSV);
** = less common;
* = rare [from reference 4] Adapted from reference 6

Of the multiple viral causes of encephalitis, it is important to diagnose HSV encephalitis (HSE), one of the commonest brain disorders in immunocompetent individuals.[9] It is important to diagnose HSE because there is specific anti-viral therapy available. Early diagnosis of HSE is essential, as the rapid initiation of anti-viral therapy is required to minimize morbidity. Although acyclovir represents a significant improvement in therapy, it is still not adequate as many patients who are treated appropriately still have significant neurological impairment as a result of infection.[10]

HSE often has a prodrome of fever, nausea, and headache of a few days duration.[7] In this case, the illness preceding the admission to hospital had the features of the HSE prodrome. HSE often presents as an acute illness with an altered level of consciousness and non-specific neurological findings. In addition, a relapsing and remitting encephalitis is one unusual presentation of HSE which has been described.[7] The patient in this case was unusual in that her illness followed a remitting and relapsing course.

SIADH occurs in some cases of HSE.[4] On the fifth day in hospital, this patient developed hyponatremia. Although the mechanism is not known, involvement of the hypothalamic-pituitary axis in the course of HSE infection could account for the inappropriate release of ADH leading to excess water retention and sodium dilution. Other potential causes of the hyponatremia include ECF volume depletion, temporary impairment of water diuresis (eg. due to pain or emotion), and medications.

In the acute phase of HSE, the CSF demonstrates mild to moderate pleocytosis (5-500 cells/mm^3) mainly consisting of mononuclear cells. The protein in the CSF may be normal or be increased up to 2 g/L.[7] The results of the lumbar puncture performed on the fourth day in hospital showed moderate mononuclear cell pleocytosis and increased protein.

EEG has been used to attempt to diagnose HSE. There is non-specific slow-wave activity during the first five days of the illness. As the illness progresses, paroxysmal sharp waves or triphasic complexes with temporal predominance can be found.[7] These findings are of little use in diagnosing HSE during the critical early stages of the disease.

In HSE, medical imaging studies performed a few days after the onset of symptoms, show low density lesions in the CT of the brain in 70% of cases.[7] Fronto-basal and temporal lesions can be shown by MRI as hypointense lesions on T1-weighted images and hyperintense lesions on proton density and T2-weighted images at an earlier stage than by CT, suggesting that MRI is the imaging method of choice in HSE.[7] These findings are suggestive of HSE, but are not specific.[7] In this case, the results of the medical imaging studies are consistent with these characteristic findings.

In 1989 the diagnostic dilemma presented by focal encephalopathic processes led to the recommendation that brain biopsy was a useful diagnostic approach.[6] While invasive, this procedure was considered safe with no mortality and low morbidity (1.4%).[6] In the clinical setting, brain biopsies were adopted as the gold standard for diagnosis as the isolation of HSV from the brain tissue is 99% sensitive and 100% specific.[10] A premium was placed on an accurate diagnosis as the old treatment with vidarabine had a higher risk of adverse side effects.[11] There was considerable reluctance to perform brain biopsies in the clinical setting, so the quest for alternative diagnostic procedures culminated in the use of PCR.[6]

The diagnostic procedure performed in this case was likely a PCR analysis of the CSF for evidence of HSV-1 DNA. HSV-2 is rarely a cause of HSE in adults, however it must be considered in infants.

Anti-viral therapy with acyclovir was started on the third day of her hospital admission, at which point the patient was severely obtunded. Given the rocky clinical course it would be interesting to know this patient's outcome.

Pathological Discussion

The diagnostic procedure was polymerase chain reaction (PCR) amplification of HSV-1 sequences from the patient's cerebrospinal fluid. The sensitivity and specificity of PCR for the detection of HSV-1 encephalitis are >95% and virtually 100%, respectively.[10] Serological studies involving the detection of HSV antibodies in the CSF are both sensitive and specific, especially when the assay is corrected for non-specific leakage across the blood-brain barrier. Unfortunately, the antibody assays generally

do not become positive until a week into the illness thus limiting their applicability. Definitive diagnosis of HSV encephalitis previously required brain biopsy. Although biopsy is sensitive and specific, it is invasive and associated with morbidity. There must be a high clinical suspicion of HSE before a PCR test is ordered. This is because the false positive rate is significant and may cloud the real diagnosis. Furthermore, the PCR test must be performed by a facility with expertise in this area as the test is easily contaminated.

HSV encephalitis is the most common cause of sporadic acute encephalitis in the western world. The annual incidence of HSE is estimated at between 1:250000 and 1:1000000 of the population, making HSE one of the commonest brain disorders of immunocompetent individuals.[9] HSV-1 and HSV-2 account for 90% and 10% of cases, respectively.[9] HSV infections of the CNS remain common and a high index of suspicion is warranted in the patient presenting with encephalopathy, particularly with focal neurological findings. It is not uncommon to get meningitis from a primary HSV-2 infection. This resolves spontaneously, and does not resemble this case.

The clinical presentation of HSE can be confused with a number of different conditions, and historically it was considered a difficult disease to diagnose.[6] Illustrating this point is a NIAID study from 1989 which focussed on 432 patients who underwent a brain biopsy for a presumptive diagnosis of herpes encephalitis.[6] In only 45% of cases was the herpes virus isolated from the brain biopsy samples, 22% of the people were diagnosed with conditions other than herpes encephalitis, and the diagnosis of 33% were not determined.[6] Table 4 lists the conditions which were found in the 95 patients with alternative confirmed diagnoses. In the majority of these patients focal neurological deficits were identified.

The acute phase of HSV-1 encephalitis is characterized by rarefaction necrosis, hemorrhage and edema commonly involving the inferior and medial regions of the temporal lobes and the orbital gyri of the frontal lobes. Sequelae of severe brain swelling are potentially fatal and include compression of ventricles, shift of midline structures, tentorial herniation, and compression of the midbrain. In the early stages, histolgy reveals microglial hyperplasia and infiltration of meninges and blood vessels with lymphocytes, mononuclear cells and plasma cells (Figure 2). Infiltration of blood vessels accompanied by necrotizing changes leads to the characteristic histological change referred to as perivascular cuffing. Cowdry intranuclear inclusion bodies may be found in both neurons or glia although they are often difficult to detect (Figure 3). Intranuclear inclusions may be highlighted by immunostaining (Figure 4). Upon ultrastructural examination, the ensembled

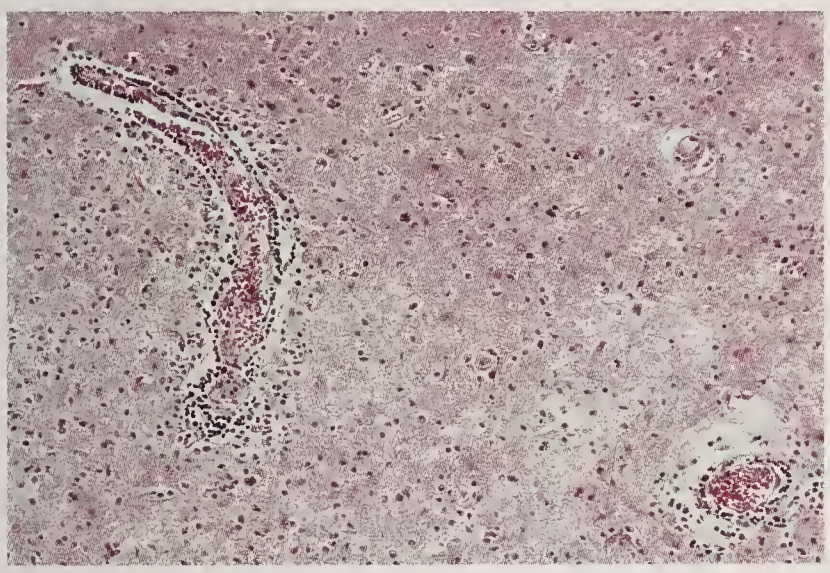

FIGURE 2. *Sleeves of lymphocytes around blood vessels in an area of patchy necrosis and edema - brain biopsy (H and E). Slide provided courtesy of Dr. Bilbao, SMH.*

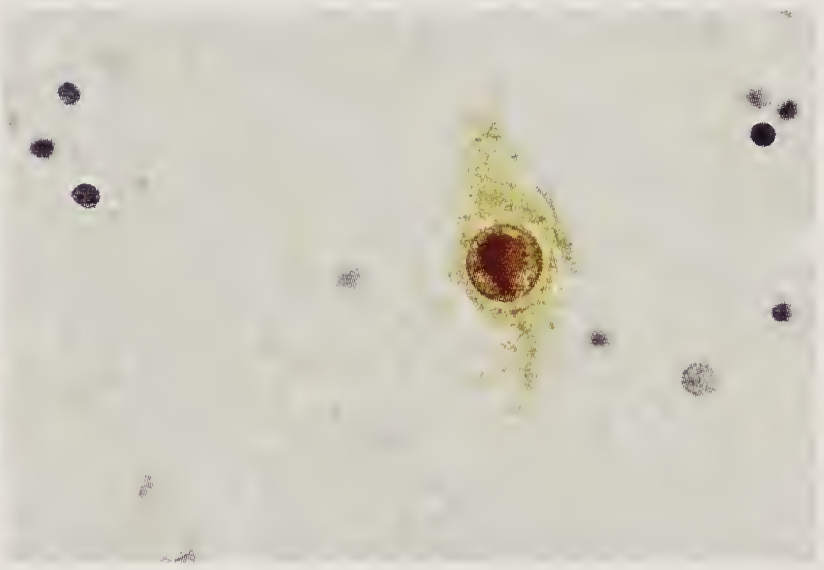

FIGURE 4. *Immunoperoxidase technique using antibodies against HSV helps in the identification of inclusion bodies (oil immersion). Slide provided courtesy of Dr. Bilbao, SMH.*

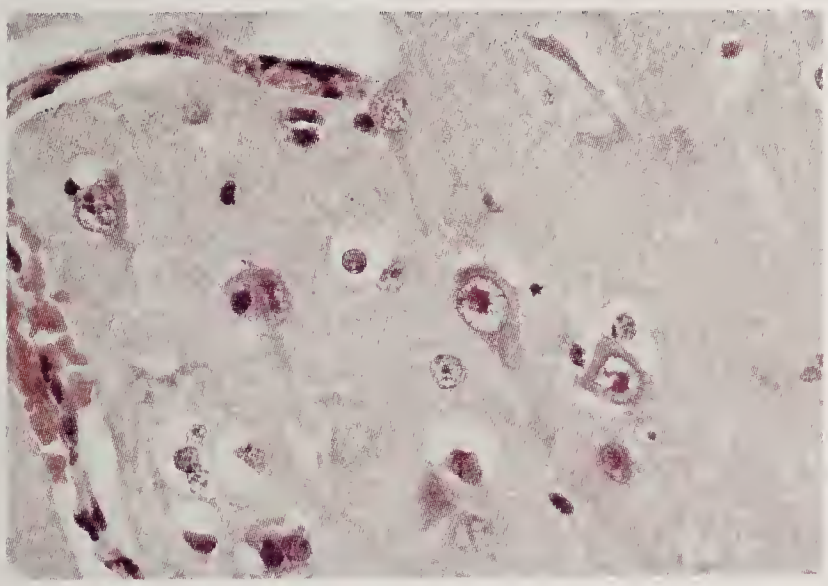

FIGURE 3. *Neuronal intranuclear inclusions are characteristic of HSV-1 encephalitis (oil emersion). Slide provided courtesy of Dr. Bilbao, SMH.*

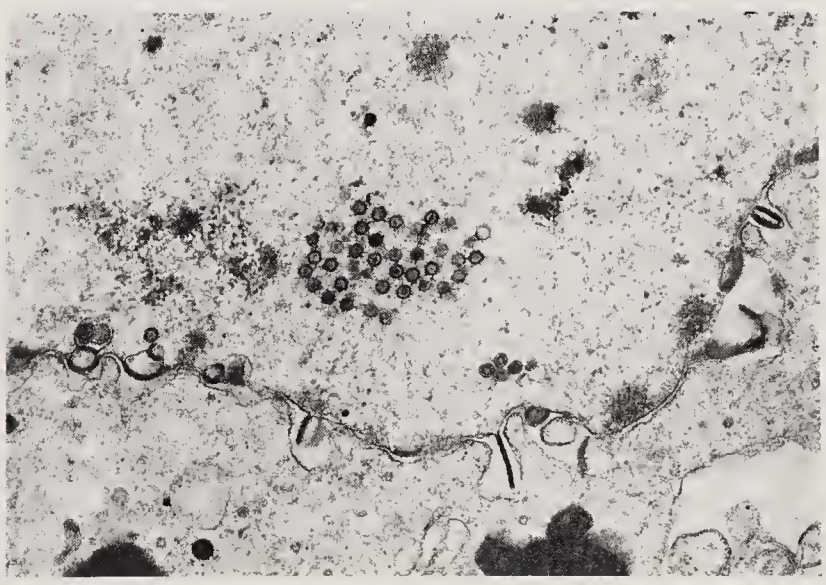

FIGURE 5. *Clusters of intranuclear nucleocapsids and "budding" virions from the nuclear membrane (electron micrograph). Slide provided courtesy of Dr. Bilbao, SMH.*

HSV-1 particle appears as an icosahedral nucleocapsid measuring 10-120 nm in diameter. The virion envelope is acquired from the host cell nuclear membrane (Figure 5).

HSV-1 encephalitis may occur either as a result of primary infection or reactivation of a latent HSV-1 infection. Potential sites of latency include the trigeminal ganglion or within the brain itself. It has been postulated that in some cases the virus enters the brain via olfactory pathways. Entry of the virus into the CNS via meningeal branches of the trigeminal nerve or olfactory pathways has been invoked to explain the selective destruction of limbic structures seen in HSV-1 encephalitis. Perhaps a more plausible explanation for this localization of infection is that chemical and immunological properties unique to the limbic system enable the HSV to manifest its destructive behaviour.[13]

Untreated HSV-1 encephalitis is often fatal. Acyclovir significantly improves prognosis, however, neurological sequelae are present in an unacceptable number of cases. New anti-HSV agents are in development. The incidence and severity of sequelae are related to the age of the patient and the level of consciousness at the time of initiation of therapy. Clinical suspicion of HSV encephalitis warrants therapy with acyclovir prior to definitive diagnosis, as it has low toxicity in patients with normal renal function and any delay in the initiation of therapy likely worsens prognosis. A definitive diagnosis of HSV encephalitis can then be made with PCR. HSV DNA sequences are detectable with PCR for up to five days following initiation of acyclovir therapy.[9] Approximately 5-10% of patients with HSV encephalitis will clinically relapse.

Patient's Outcome

During the week following the diagnosis of HSE, the patient began to make a recovery. As soon as the PCR test was positive for HSV-1 (24 hr) and the CSF culture and sensitivity cultures were negative, the ceftriaxone and ampicillin were discontinued. She could be aroused, opened her eyes spontaneously and followed simple commands. On the tenth day in hospital, the patient experienced a sudden deterioration marked by the onset of choreiform activity and clonic movement of both arms. EEG studies showed epileptiform activity in the left frontal and right temporal, frontal, and parietal areas. The seizures resolved after the administration of 5 mg of valium. The patient was placed on phenytoin.

Following this deterioration, the patient began to recover rapidly. After two days, she was verbalizing, naming, following commands, and repeating. There was no longer focal weakness. A cognitive assessment performed approximately one week later revealed diminished attention span, short and intermediate term memory, spatial awareness and manipulation of acquired data. Inappropriate staring spells, likely due to complex-partial seizures, were noted.

Several weeks later, the patient experienced an episode of recurrence of some of her previous symptoms associated with the development of pneumonia. There were involuntary movements, decreased level of consciousness and fever. Most of these symptoms resolved rapidly. After a few months the patient had regained most of her cognitive functions, however she did feel 'slower' and found her memory was not as good.

Further Discussion

Seizures occur in more than 50% of patients with severe encephalitis.[12] HSE is commonly associated with complex-partial seizures. Complex-partial seizures originate in the medial or lateral part of the temporal lobe or hippocampus. These are regions selectively damaged in HSE. Complex-partial seizures are manifested clinically by visceral, motor, or affective disturbances. In this case, the partial seizures evolved to tonic-clonic convulsions. This occurs as a result of the spread of seizure activity to the thalamus and upper reticular formation, and secondarily spread to the entire cerebral cortex.

Clinical relapse of HSE several months after the initial occurrence in patients treated with acyclovir has been reported.[3] Several mechanisms may be responsible for relapse including incomplete treatment of the initial infection and autoimmune post-infectious encephalopathy. One series has demonstrated that HSV DNA is not detectable by PCR in CSF fluid during recurrences occurring one month or more after the initial infection.[3] This suggests an autoimmune etiology for such recurrences. Earlier relapse seems to be due to incomplete therapy. In this case it is possible that the fever, loss of consciousness and convulsions experienced by the patient were not due to relapse but rather to sepsis. Conversely, cytokines released during the acute phase of the pneumonia may have modulated this patient's immune response predisposing her to a post-herpetic encephalopathy.

Summary

A high index of suspicion of herpes simplex encephalitis should be entertained in any person presenting with acute onset of a febrile illness with focal neurological deficits. The speed with which acyclovir is started is an important prognostic factor for the morbidity and mortality associated with this illness. PCR detection of HSV DNA in the CSF is the appropriate investigation only when there is a strong clinical suspicion of HSE.

Acknowledgements

The authors are indebted to the following for their assistance in editing this manuscript: Dr. M. Louie and Dr. A. Simor, Infectious Diseases, Sunnybrook Health Sciences Centre; Dr. R. Farb, Radiologist, Sunnybrook Health Sciences Centre; Dr. J. Bilbao, Pathology, St. Michael's Hospital.

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Hematology Rounds

Kelly Grant, BSc. (0T0) and Ali Islam, BSc. (9T9)

A 72 year old woman presents to her family doctor complaining of a six month history of back pain that is worse with movement. The patient also admits to being increasingly tired over the past six months, and has had a 15 pound weight loss over this period.

The patient has no other complaints. She has never smoked and does not drink regularly. She has had no change in respiratory function or bowel habits and has neither abdominal nor pelvic pain. She has no past history of cancer. She does not take any medications.

On physical examination, there was tenderness at the level of L2 in the lumbar region of the spine. There were no distal focal neurological deficits and reflexes were normal. Rectal tone was normal and there was no saddle anesthesia. There was no tenderness or palpable masses in the breasts or abdomen, and no abnormalities noted on pelvic and digital rectal examination.

A spinal X-ray was performed (not shown), and the results revealed a compression fracture at L2.

To further investigate the cause of this pathological fracture, a CBC and differential (Table 1) and blood smear were ordered. The following results were obtained from the laboratory:

Table 1
Laboratory Values

CBC	Units	Reference Values
WBC	5 x 10^9/L	4-11
HBG	104 g/L	120-160 (F)
MCV	94 fL	80-98
PLT	200 x 10^9/L	150-400

No abnormalities in the differential.

Blood smear shows normocytic and normochromic red blood cells. Rouleaux formation of red blood cells was present.

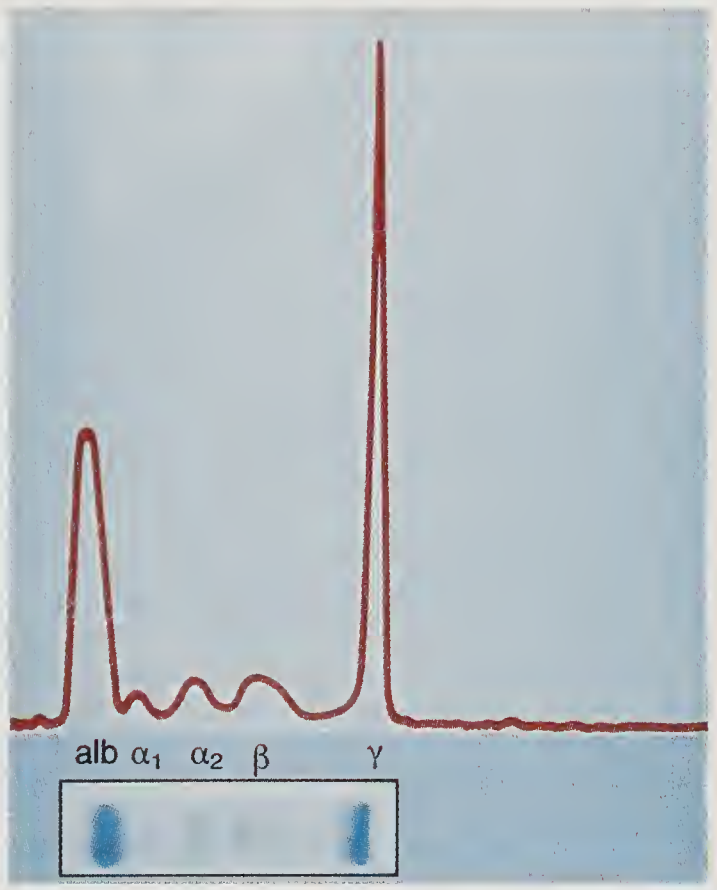

FIGURE 1. Serum protein electrophoresis.

Given this information, a serum protein electrophoresis (Figure 1) was ordered.

What does the gamma globulin spike represent in the serum electrophoresis?

Given the presence of the gamma globulin spike, a serum immunoelectrophoresis was also performed. The laboratory report came back as follows:

Presence of a monoclonal IgG kappa protein in the serum.

Given the history and laboratory results, what is the most likely cause of the patient's symptoms?

Answers

Back pain is an extremely common complaint seen in a family medicine practice. In a 72 year old post-menopausal woman, the most likely cause of back pain is osteoporosis or degenerative disk disease. However, the presence of fatigue and weight loss make it necessary to rule out a more ominous cause of the back pain, such as metastatic bone disease or other malignancies. The pathological compression fracture suggests that further investigation for a malignancy is required.

The search for a primary malignancy began with a thorough history and physical exam; this did not reveal any red flags. The blood work showed a normocytic, normochromic anemia with Rouleaux in the peripheral blood smear (Figure 2). The abnormal finding of Rouleaux warrants further investigation of a hematological malignancy. Rouleaux is stacking of red blood cells due to an increase in serum protein in myelomatous states. The presence of Rouleaux and a pathological fracture make multiple myeloma the working diagnosis. When suspected, investigation of multiple myeloma should include a serum protein electrophoresis.

As shown in the above results, there is a gamma globulin spike in the serum electrophoresis (Figure 1). Normally, the wide variety of immunoglobulins in the serum move heterogeneously in the electric field, so that a broad peak in the gamma region forms. In the presence of a secreting tumour, there is a sharp spike in the gamma region due to the predominance of a single product from the clonal population of plasma cells.

The nature of the spike is variable in different plasma cell disorders. The spike may consist of intact antibody of any heavy chain subclass, an altered antibody or fragment, or an isolated heavy or light chain. When light chains are filtered by the kidney, they appear in the urine as Bence-Jones protein. This can be detected by a spike in a urine electrophoresis. In about 20% of cases of multiple myeloma, the excess gamma globulin will not be detected in the serum, but light chains will be found in the urine. Therefore, a urine electrophoresis should also be done when investigating the patient for multiple myeloma.

Confirmation that the protein causing the spike in the serum and/or the urine is monoclonal requires an immunoelectrophoresis. As indicated by the laboratory report, there was a monoclonal IgG kappa protein in the serum. Given this information, it appears that the most likely diagnosis in this patient is multiple myeloma.

Discussion

The definition of multiple myeloma is a malignant proliferation of plasma cells derived from a single clone. Presumably, the malignant plasma cells acquire a proliferation advantage by failing to undergo apoptosis.[1] The disease accounts for 10% of all hematological malignancies and is responsible for approximately 10,000 deaths each year in the United States.[2] It is largely a disease of the older population with a median age of 60 years at diagnosis, although it can occasionally be seen in younger individuals. Blacks are affected twice as frequently as whites, but the factors for this difference in incidence is unknown.

A number of organ dysfunctions and symptoms of bone pain or fractures, renal failure, anemia, hypercalcemia, and

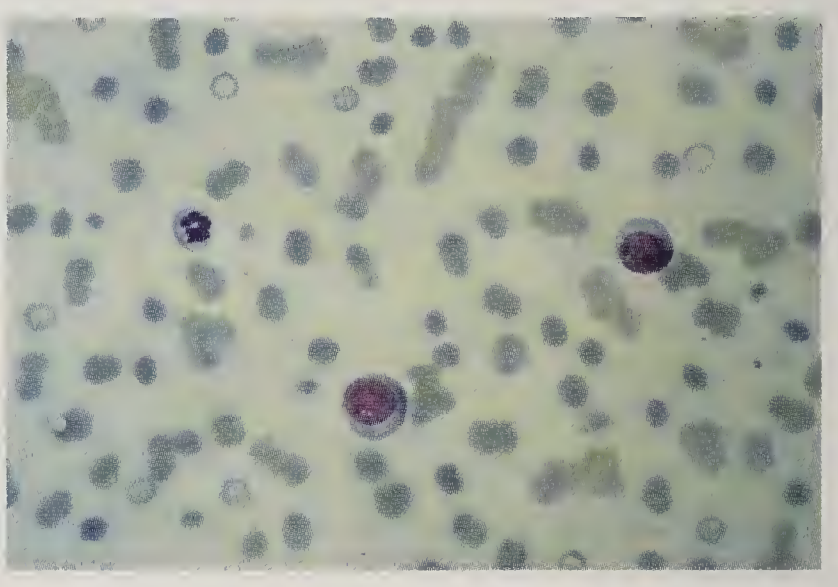

FIGURE 2. *Peripheral blood film showing red blood cells in Rouleaux formations.*

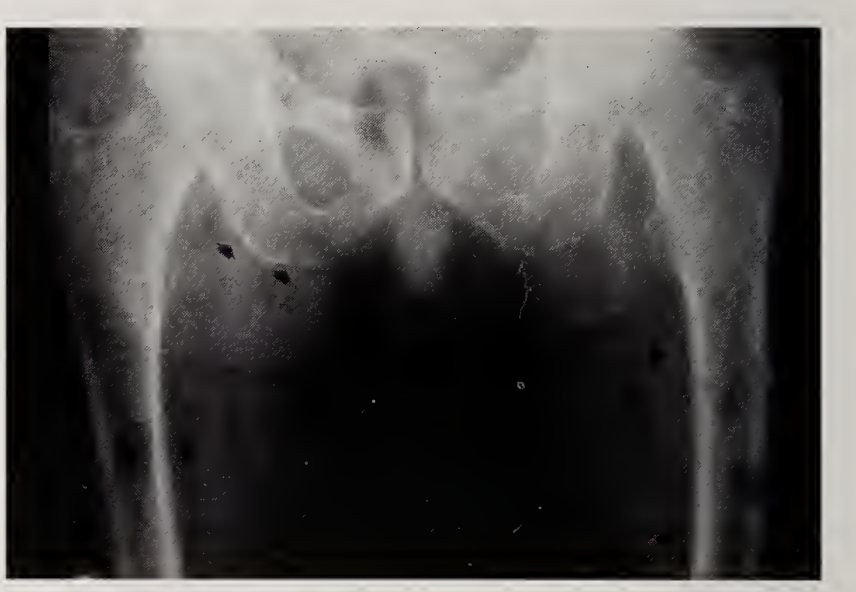

FIGURE 3. *Arrows indicate characteristic lytic bone lesions seen in multiple myeloma.*

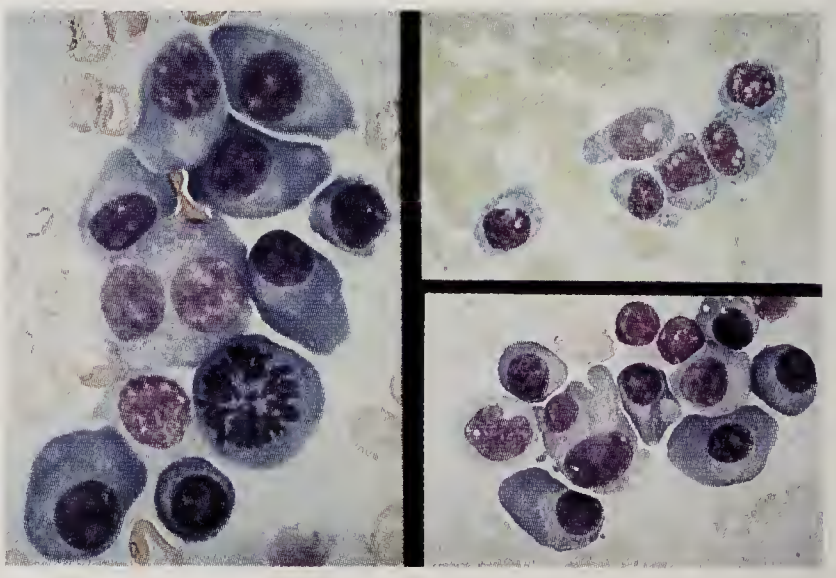

FIGURE 4. *Bone marrow aspirate showing abnormal plasma cells.*

susceptibility to infections may result from the presence of the tumour, its products, and/or the host response to the tumour.[3] Bone pain is the most common symptom, affecting almost 80% of patients.[4] The characteristic lesions shown in Figure 3 are caused by proliferation of the tumour cells and the activation of osteoclasts by myeloma cells that subsequently destroy bone. The bone lesions are lytic, and are rarely associated with new bone formation. The bone lysis leads to calcium mobilization; hypercalcemia may result and cause renal damage.

There are changes in the bone marrow that are characteristic of multiple myeloma. Plasma cells usually make up less than 5% of bone marrow cells. In multiple myeloma, greater than 10% of the cells are plasma cells.[5] Some of the plasma cells have abnormal morphology with binucleated and multinucleated forms. The plasma cells often appear immature and tend to cluster together in sheets as shown in Figure 4. The anemia, which often occurs in multiple myeloma, can be explained by bone marrow infiltration with myeloma cells. The type of anemia observed in myeloma is usually classified as normocytic and normochromic. It is caused by both the replacement of normal marrow by expanding tumour cells and the inhibition of hematopoiesis by factors made by the tumour.

Susceptibility to bacterial infections is increased with multiple myeloma. This is a result of severe hypogammaglobulinemia due to decreased production and increased destruction of normal antibodies.[6] For unknown reasons, myeloma patients also tend to have low CD4+ counts, low granulocyte lysozyme content, and abnormal compliment functions. Together, these factors all contribute to the immune deficiency state of myeloma patients.

Renal failure is another serious and common complication of multiple myeloma. There are several factors that lead to renal pathophysiology.[7] Tubular interstitial disease is the most common cause of renal failure due to excess light chains filtered by the kidney. Hypercalcemia, recurrent infections, and occasional infiltration of tumour cells are other causes of renal failure.

A benign condition that leads to increased monoclonal protein in the serum is known as monogammopathy of undetermined significance (MGUS). In this condition, there are no abnormal blood counts, bone lesions, hypercalcemia, or renal failure. The frequency of MGUS increases with age, and 10% of people with MGUS develop multiple myeloma within ten years. These patients should be monitored for changes in their condition.

It is evident that multiple myeloma has widespread effects on different organ systems. Many of the clinical features of myeloma can present as medical emergencies such as pathological fractures, renal failure, hypercalcemia, and infection, and appropriate management must follow. Management of the disease may include chemotherapy, radiotherapy, bisphosphonates to prevent bone reabsorption, hydration for renal failure, and antibiotics for infections.[8] This management leads to significant palliation and improvement in the complications seen in myeloma. However, despite these measures, multiple myeloma is incurable, with a median survival of 3-4 years.

Acknowledgements

We would like to thank Dr. J. Brandwein for helping with this case.

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Inflammatory Bowel Disease Crohn's Disease vs. Ulcerative Colitis

Dan Comay, BSc. (9T9)

Inflammatory Bowel Disease (IBD) is a chronic inflammatory condition of the gastrointestinal tract of unknown etiology. It is the collective term given to both Crohn's Disease (CD) and Ulcerative Colitis (UC). IBD generally presents before age thirty, occurs equally in males and females, is more common in Jews than non-Jews and has a familial tendency. The typical presentation may involve abdominal pain, fever, diarrhea and rectal bleeding.

Once a diagnosis of IBD is suspected, the first step is to rule out infectious causes, such as *Campylobacter, Chlamydia, Entamoeba histolytica, Yersinia enterocolitica* and *C. difficile.* The next step is to differentiate between CD and UC. Although the medical treatments of CD and UC are similar, their respective complications and prognoses have important differences. Accurate differentiation between CD and UC is essential for effective management.

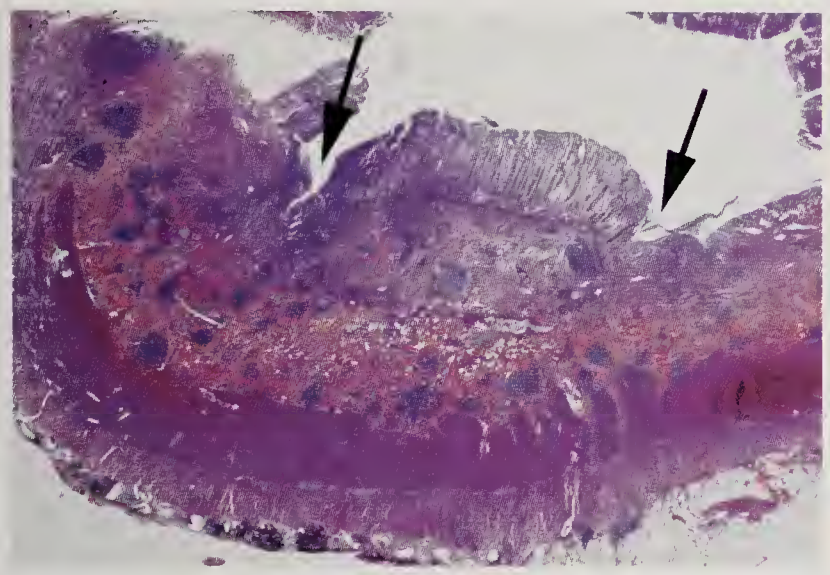
An approach to distinguishing between CD and UC starts with understanding the key histopathological differences. From these differences arise the characteristic features seen radiologically and endoscopically. This section will highlight the principle morphological differences between CD and UC and demonstrate how these differences correlate with the radioscopic and endoscopic findings.

Acknowledgements

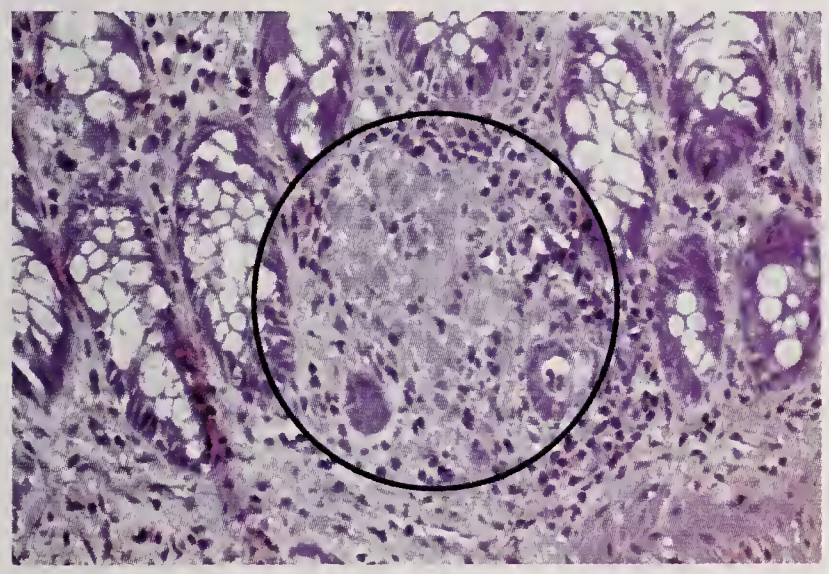
I would like to thank the following contributors who graciously lent their images and their knowledge: Dr. J. Cullen, Dr. G. Kandel, Dr. G. Gardiner, Dr. T. Moore, Dr. A. Zalev and Steven Sears (9T8). These images can also be found in the Gastroenterology section of DigiDoc: *The Sights and Sounds of Internal Medicine.* For more information, please visit http://icarus.med.utoronto.ca/digidoc/digimain.html.

Crohn's Disease

Histology



Transmural involvement. *Note the thickening of the entire bowel wall, the deep mucosal fissure ulcers (arrows) and numerous transmural lymphoid aggregates.*



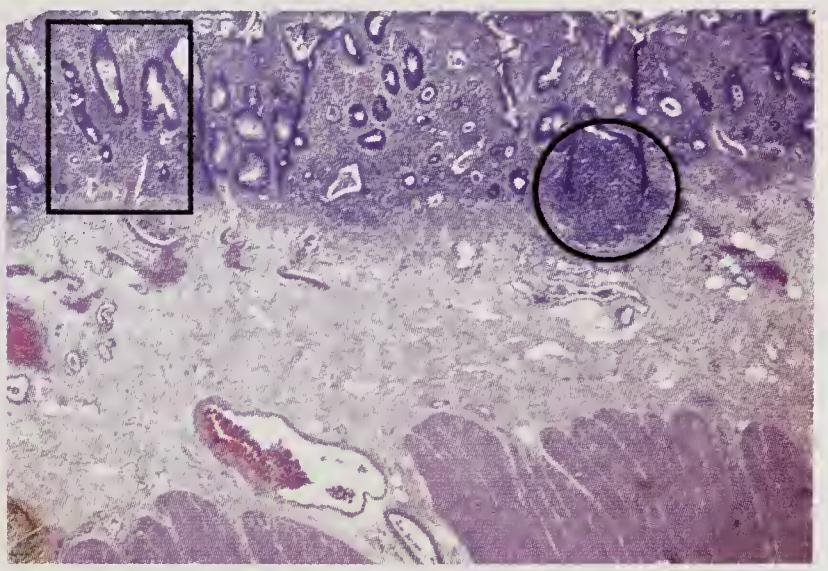
Granuloma. *A single non-caseating granuloma (circle) is characteristic of CD and is not typically found in UC.*

Pathology

Skip lesions *refer to the discontinuous involvement of the bowel in CD. This segment of stenosed bowel caused obstructive symptoms in the patient.*

Ulcerative Colitis

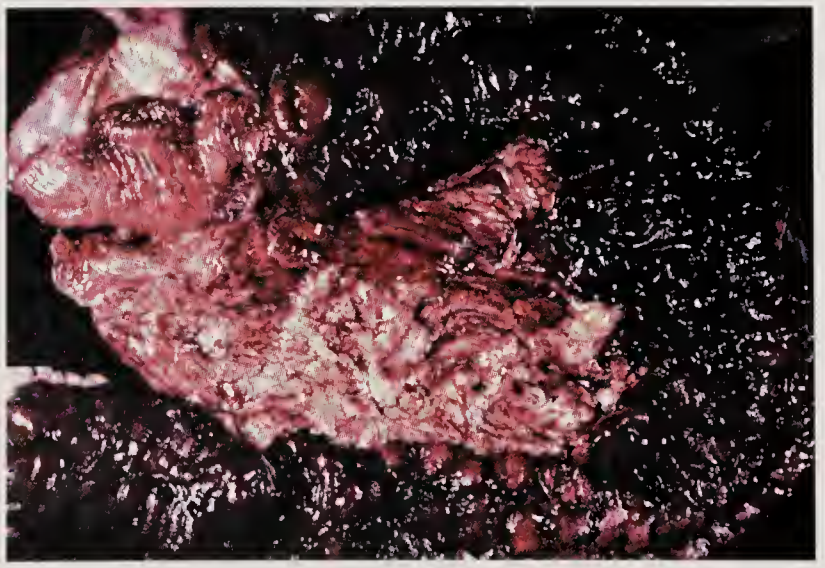
Histology



Mucosal involvement. *The inflammatory process is limited to the mucosa in UC. Note the lymphoid aggregate (circle), mucosal gland shortening and branching (box) and expanded lamina propria.*

Pseudopolyps. *An inflammatory pseudopolyp (circle) is formed as mucosa is ulcerated and denuded, leaving a polypoid island of intact mucosa.*

Pathology

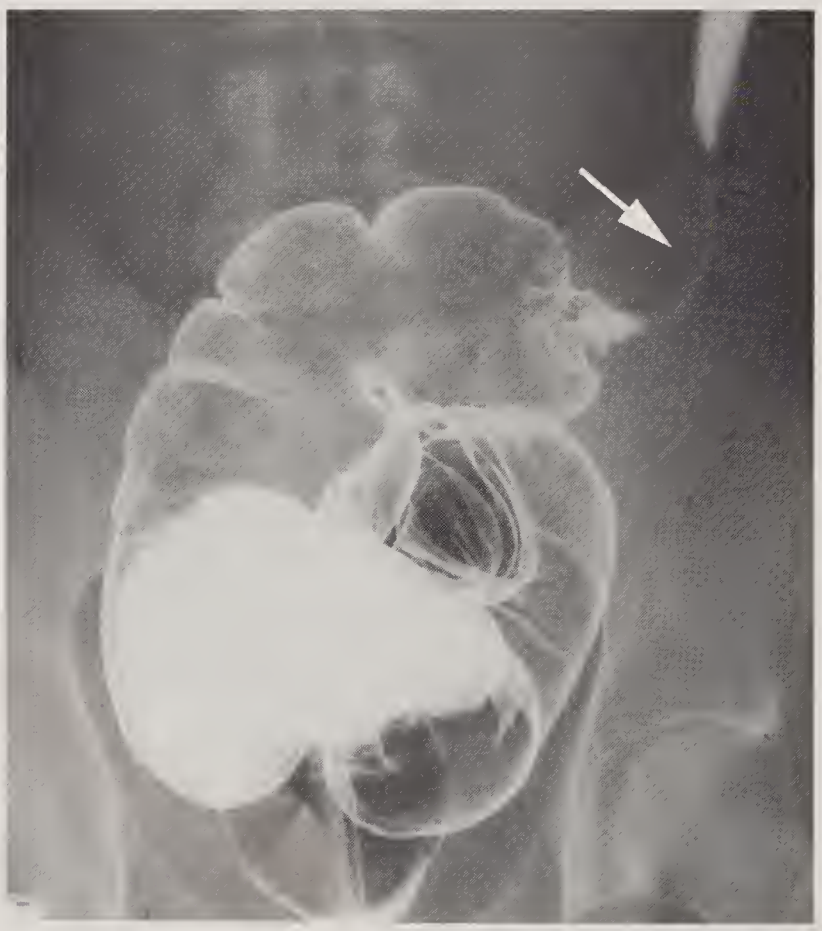


Continuous involvement. *The mucosa is hyperemic and edematous (inflammed) from the distal left colon extending proximally (there are no "skip lesions" in UC).*

Crohn's Disease

Radiology

Terminal ileitis. *Inflammation and thickening of the terminal ileum (with sparing of the rest of the bowel). Note the appendix filled with barium just lateral to the affected ileum.*



String sign. *The stenosed segment of bowel shown above produces a classic "string sign" (arrow) as only a thin stream of barium is able to pass through the obstruction.*

Ulcerative Colitis

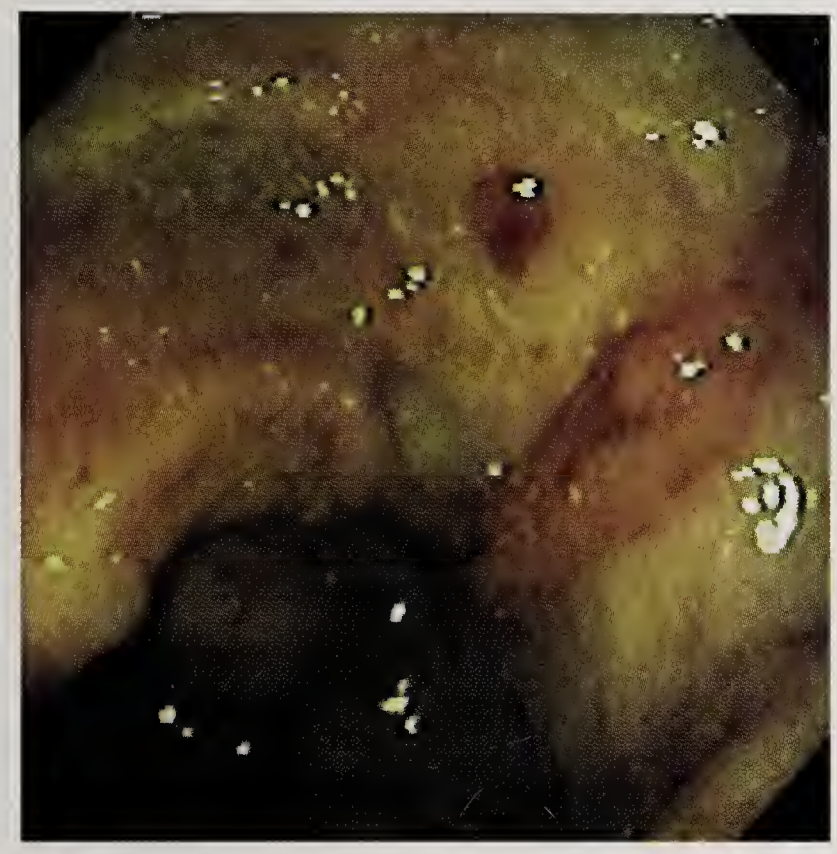
Radiology

Numerous pseudopolyps create filling defects extending proximally, encompassing the entire colon.

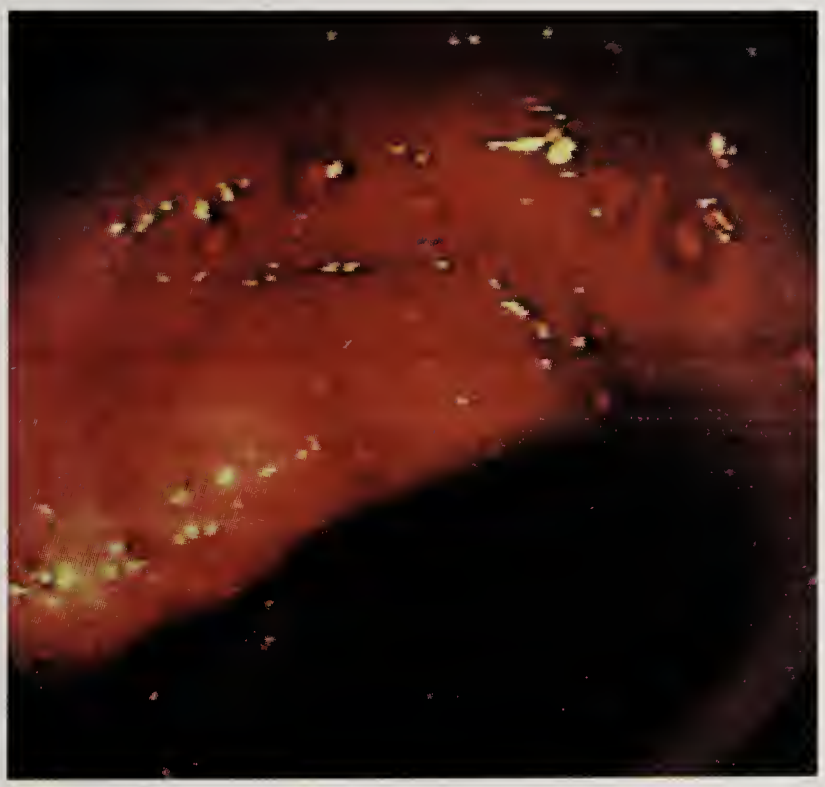
Left sided loss of haustral folds and numerous pseudopolyp filling defects (box).

Crohn's Disease

Endoscopy



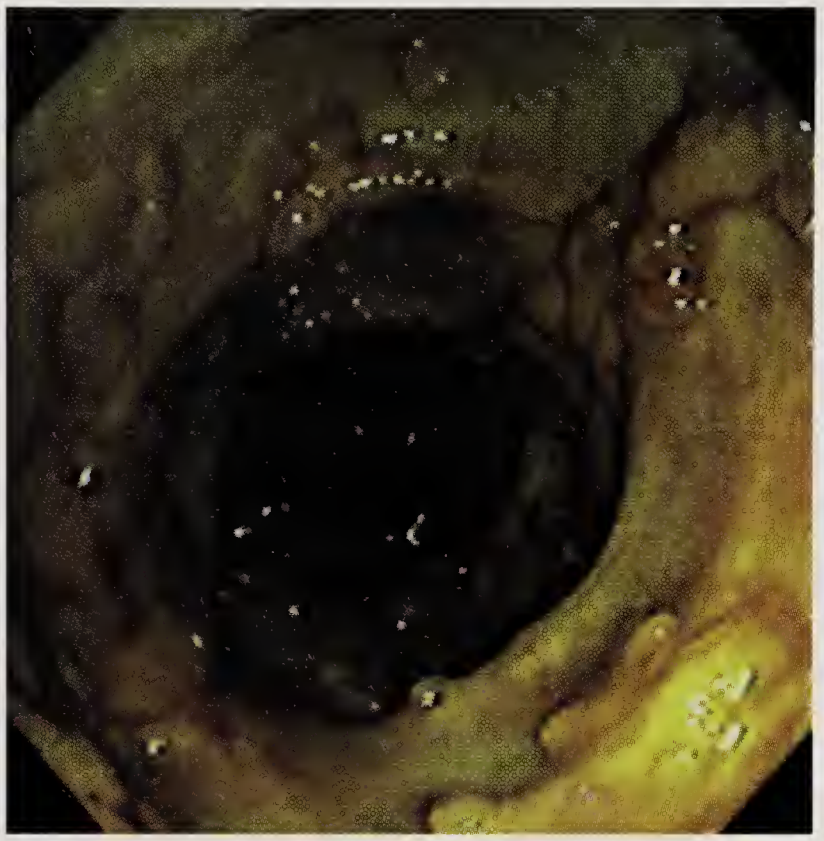
Mucosal ulcers. *Single mucosal ulcer and a linear ulcer (oriented along the axis of the bowel).*



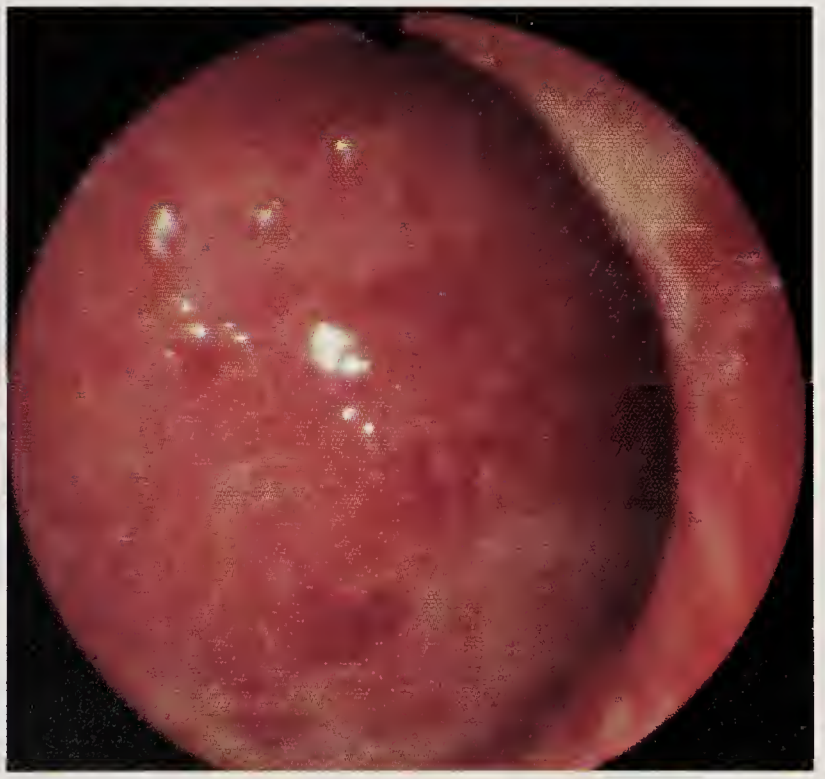
Aphthous ulcers. *Several aphthous ulcers (white lesions on a red base) are seen here speckling the mucosa.*

Ulcerative Colitis

Endoscopy



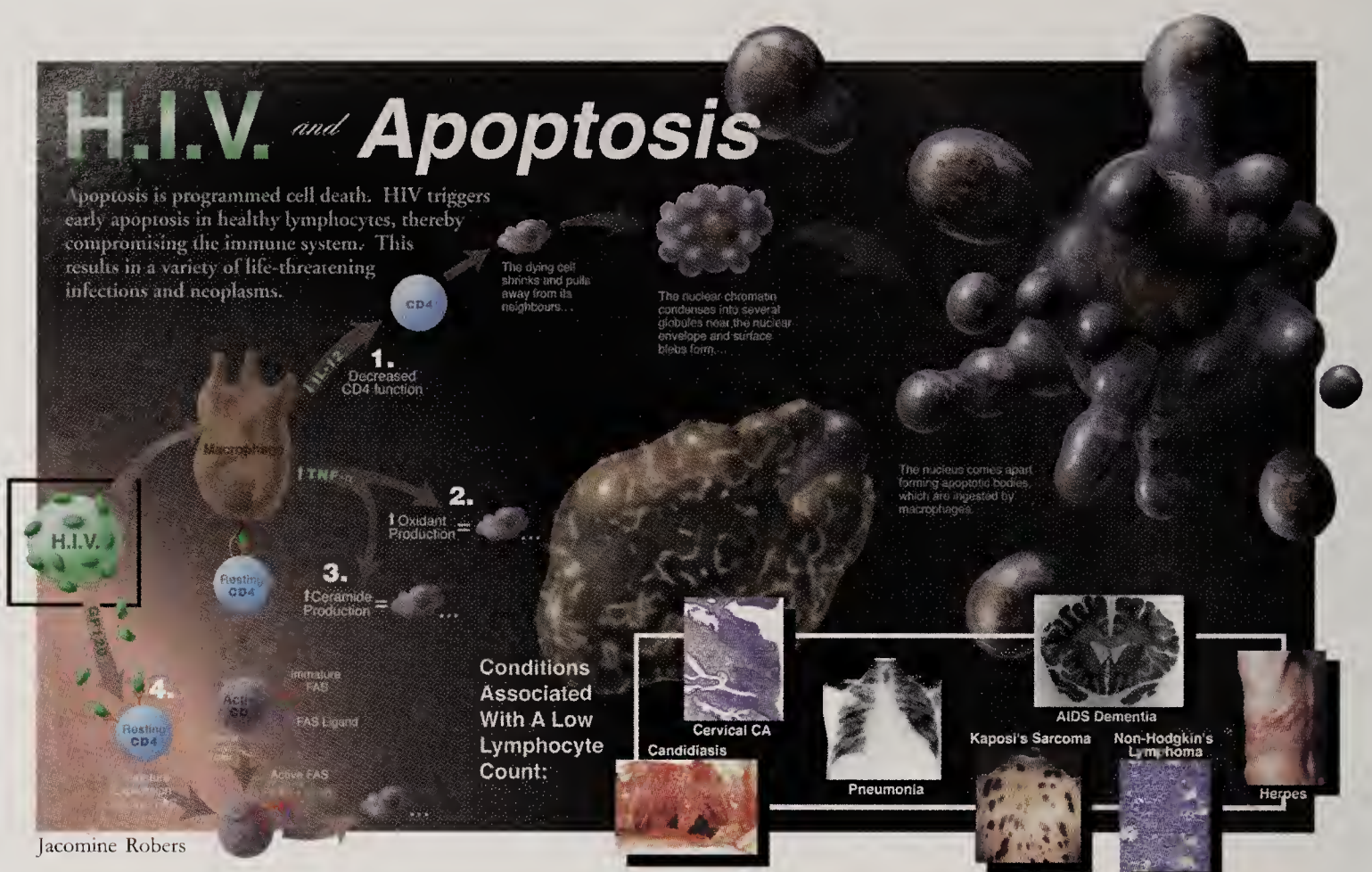
The mucosal layer is completely ulcerated except for islands of intact mucosa (pseudopolyps).



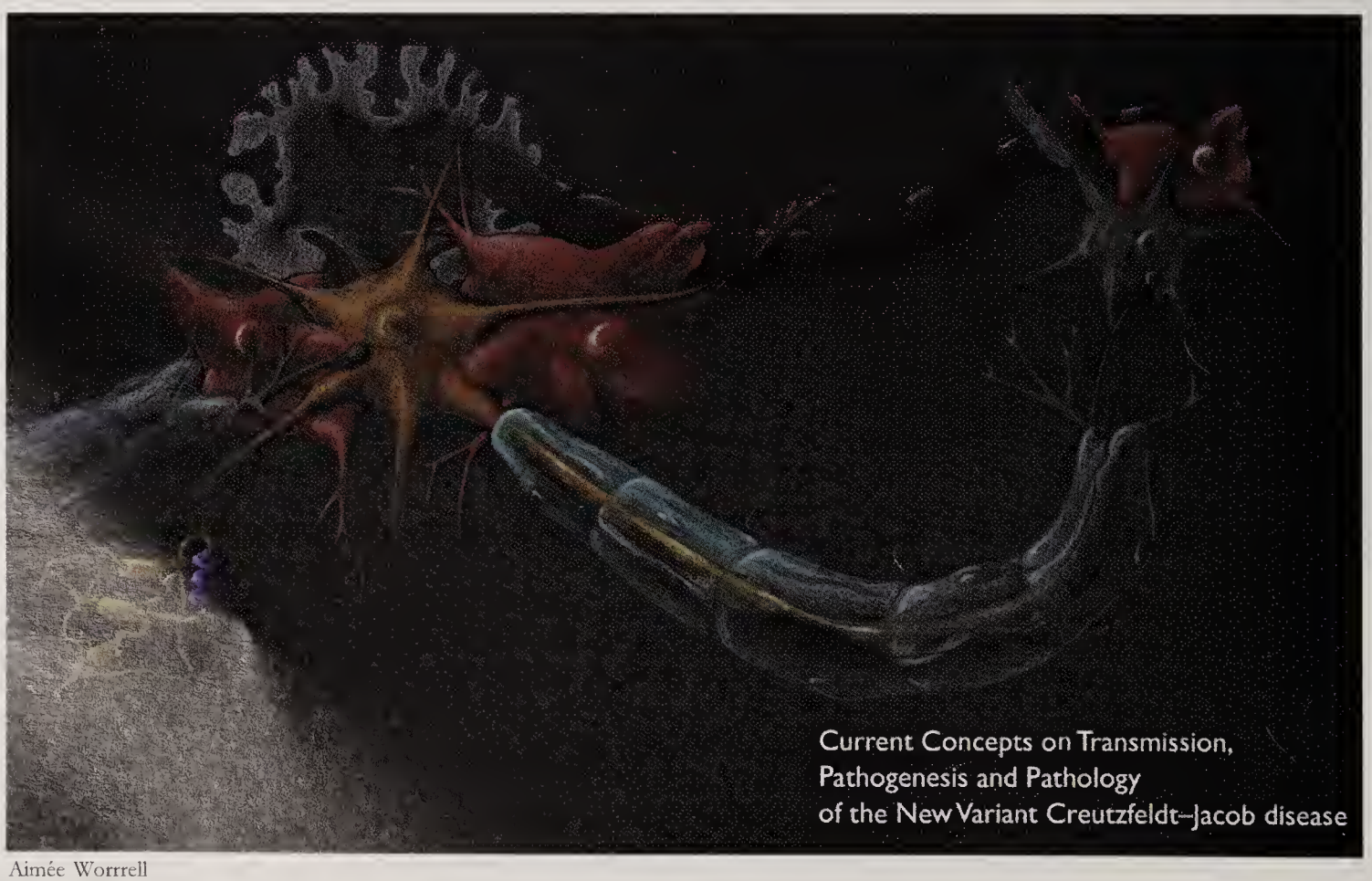
Friable, hyperemic and edematous appearance of the bowel wall in UC.

Biomedical Communications Gallery

Perusing through a *UTMJ,* one realizes that images play a large role in complementing the text. In particular is the skilled work of medical illustrators which has been a major feature of the *UTMJ* since the early 1970s. This enormous responsibility has fallen on the shoulders of the students in the Department of Surgery's, Division of Biomedical Communications (BMC). Formerly known as Art as Applied to Medicine, students of BMC have used visual communication that is didactic, accurate and esthetically pleasing to teach thousands of students and faculty everything from the basics of anatomy to the most complex of pathologies and surgical procedures for over fifty years. Here we present samples of BMC's 1998 graduating class.

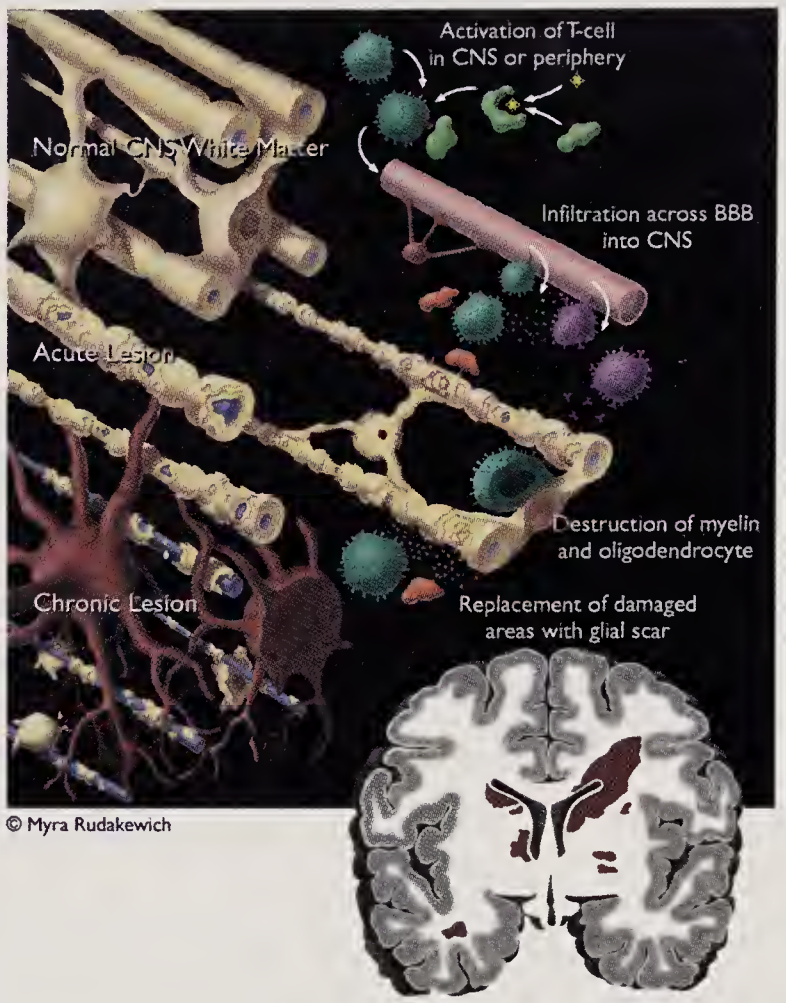

H.I.V. and Apoptosis
Apoptosis is programmed cell death. HIV triggers early apoptosis in healthy lymphocytes, thereby compromising the immune system. This results in a variety of life-threatening infections and neoplasms.
CD4
The dying cell shrinks and pulls away from its neighbours...
The nuclear chromatin condenses into several globules near the nuclear envelope and surface blebs form...
The nucleus comes apart forming apoptotic bodies, which are ingested by macrophages
1. Decreased CD4 function
2. ↑ Oxidant Production
3. ↑ Ceramide Production
4.
H.I.V.
Resting CD4
Macrophage
↑ TNF-α
Cytokines
Immature FAS
FAS Ligand
Active FAS
Conditions Associated With A Low Lymphocyte Count:
Cervical CA
Candidiasis
Pneumonia
AIDS Dementia
Kaposi's Sarcoma
Non-Hodgkin's Lymphoma
Herpes

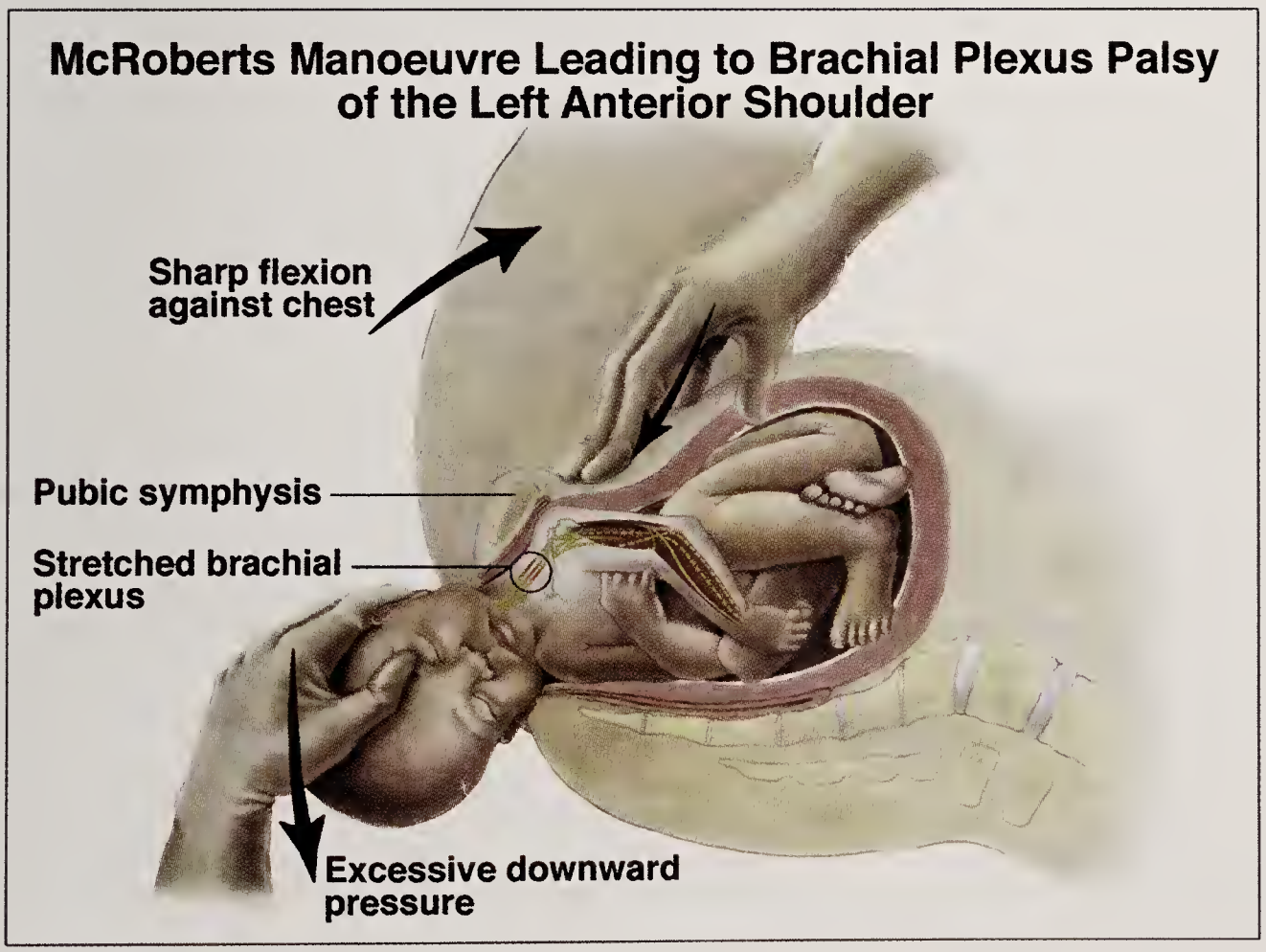
Jacomine Robers



Aimée Worrrell

Jennifer Bosy


MULTIPLE SCLEROSIS
Pathology and Postulated Mechanisms of Pathogenesis
Activation of T-cell in CNS or periphery
Normal CNS White Matter
Infiltration across BBB into CNS
Acute Lesion
Destruction of myelin and oligodendrocyte
Chronic Lesion
Replacement of damaged areas with glial scar
© Myra Rudakewich


McRoberts Manoeuvre Leading to Brachial Plexus Palsy of the Left Anterior Shoulder
Sharp flexion against chest
Pubic symphysis
Stretched brachial plexus
Excessive downward pressure

Carin Cain

It Don't Mean a Thing if it Ain't Got That Swing

Steven Shadowitz,* MDCM, FRCP(C)

Presenter: A 65 year old man presented to the emergency department complaining of a two day history of mild abdominal pain and three weeks of increasing abdominal swelling.

Dr. Shadowitz: Abdominal pain is a very common complaint, and has an exhaustive differential diagnosis. The combination of abdominal pain and swelling, however, is less common. My first approach would be to explore with the patient the nature of the swelling, rather than the abdominal pain. It is important to first distinguish whether the patient is complaining of the symptom of transient abdominal distension, such as would be experienced in lactose intolerance, or the objective sign of abdominal swelling. Clues on history to determine whether abdominal swelling is present include weight gain, change in belt, pant or skirt size, and stretch marks on the skin noticed by the patient.

P: The patient has noticed increasing abdominal girth over the last several weeks, as indicated by his pants no longer being able to fit. Before we continue with the case, can you discuss your general approach to the patient with a swollen abdomen?

Dr. S: Ah, the dreaded *Morning Report* question, what is your approach to this problem? There are several ways to attack any diagnostic question. For example, an anatomic approach works well in the approach to the surgical abdomen. An etiologic approach is summarized in the mnemonic *VINDICATE: V* for vascular, *I* for infectious, *N* for neoplastic, *D* for degenerative, *I* for iatrogenic, *C* for congenital, *A* for autoimmune, *T* for trauma, and *E* for endocrine/metabolic, and is useful, for example in the approach to fever of unknown origin. In our patient with a swollen abdomen, a pathophysiologic approach may work best. A common mnemonic used for remembering the causes of abdominal swelling is the six -F's: fat, fluid, flatus, feces, fetus, and fatal growth (i.e. cancer). This can be reduced to thinking of the abdomen as filling up with solid, liquid, or gas. "Solid" refers to tumours, such as ovarian, endometrial or gastrointestinal cancers, fat from obesity or endocrine abnormalities such as Cushing's syndrome or high dose steroid use, pregnancy (which can be ruled out in this case one hopes), or massive hepatosplenomegaly. "Liquid" refers to ascites, a distended bladder, ovarian cysts, or pancreatic pseudocysts. "Gas" refers to intestinal gas from bowel obstruction. While the most common cause of abdominal swelling in this man is ascites, each of these categories of illness has a broad differential diagnosis and needs to be explored.

P: How would you focus your interview with this patient?

Dr. S: The history can be very useful in sorting out the various possible etiologies of this patient's complaint. The history should first focus on the rapidity of onset of the swelling. Tumours, adiposity, organomegaly and ascites are slowly progressive, whereas a bladder filling up with urine or viscera filling up with gas are acute processes that should be quickly diagnosed and treated.

A thorough review for gastrointestinal symptoms will give clues to the presence of gastrointestinal malignancy and liver disease. Risk factors for liver disease should be

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ascertained; these can include alcohol consumption, high-risk sexual activity, intravenous drug use, prior history of transfusion, and a family history of liver disease. A cardiac review of symptoms, specifically asking for symptoms of congestive heart failure, may help determine the etiology if ascites is indeed present. Endocrine symptoms should be sought, as fat and fluid in the abdomen can be present in diseases such as Cushing's syndrome and severe hypothyroidism. Constitutional symptoms such as anorexia, fatigue, weight change, and fever should be elicited, and may suggest malignancy or renal disease. Lastly, past medical history and medication usage are always useful pieces of information to obtain. In short, ask everything!

P: The patient reports being well until approximately three weeks earlier, when he noted the progressive onset of abdominal swelling. He denied jaundice, pruritis, nausea, vomiting, or a change in the colour of his urine or stools. The frequency and consistency of his stools were unchanged. He was able to pass gas. He denied any high risk sexual activity such as frequent unprotected anal intercourse, sex with prostitutes, or sex with intravenous drug users. There was no history of prior transfusion, and no family history of liver disease. There was no previous history of hospitalizations, abdominal swelling, jaundice, edema or liver disease. He admitted to four glasses of red wine per day for many years. There was no history of cardiac disease and he denied chest pain, shortness of breath on exertion, orthopnea, or paroxysmal nocturnal dyspnea, but did report some lower leg swelling. He denied symptoms of dry skin, heat or cold intolerance, or alopecia. He did complain of anorexia and weight gain.

There was no medication usage, and no medically significant family history.

Dr. S: There are several bits of information that help us here. The slow progression of the swelling strongly suggests either a "solid" problem (i.e. tumour), or a "liquid" problem (i.e. ascites). The absence of bowel symptoms is against a gastrointestinal malignancy, but by no means rules it out. The history of alcohol use raises our index of suspicion for liver disease. It is important to realize that, in general, patients tend to underestimate their alcohol intake. A rule of thumb that has been passed down from generation to generation is to double the alcohol amount that the patient reports. However, I know of no factual basis for this comment. It is often necessary to obtain a corroborating history of alcohol usage from family and friends.

P: How much alcohol is too much when it comes to liver disease?

Dr. S: In general, men need to drink 80 g of alcohol, equivalent to 5 or 6 drinks per day for 10 to 15 years to develop cirrhosis.[1] Women need less, approximately 50 g or 3 to 4 drinks per day. There is much individual variability, and in some cases, cirrhosis may develop more rapidly. Cirrhosis has even been noted in teenagers who drink heavily. Once liver disease is established, any alcohol is too much. Now may be a good time in the history to explore this man's drinking habits.

P: How do you obtain a good drinking history from a patient?

Dr. S: A useful starting strategy is the CAGE questionnaire, which asks four questions related to drinking. These include: feeling the need to cut down on drinking, feeling annoyed about questions on drinking, feeling guilty about the amount of alcohol consumed, and using an eye opener in the morning. Three or more yes answers to these questions strongly increases the likelihood of alcoholism in your patient.[2] Further questions should include asking about legal problems such as drivers' licence suspension(s) and arrest(s) due to alcohol use. Lastly, the patient should be asked about the medical complications of alcoholism. These include nervous system effects (e.g. episodes of withdrawal or seizure), gastrointestinal effects (e.g. pancreatitis, malnutrition and vitamin deficiency), cardiovascular effects (e.g. atrial arrhythmias, hypertension and cardiomyopathy), endocrine effects (e.g. impotence), and musculoskeletal effects (e.g. proximal muscle weakness).

P: The patient reports feeling annoyed about questions relating to his alcohol use, and indicated that he has tried to cut down on his drinking. Furthermore, he reports one episode of an alcohol withdrawal seizure 2 years ago, and has had several licence suspensions for being over the legal limit. He denies any other symptoms or complications of alcohol use.

Dr. S: This focuses our discussion toward the causes of abdominal pain and swelling in an alcohol abuser. Using our physiologic framework, "solid" problems are usually tumours. Although all gastrointestinal tumours could occur in this gentleman, the risk of hepatocellular carcinoma is increased in people with cirrhosis.

A "liquid" problem usually means ascites. There are four major mechanisms for increased fluid in the abdominal cavity. Firstly, elevated hydrostatic (portal) pressure can lead to ascites as a consequence of cirrhosis, congestive heart failure, constrictive pericarditis, inferior vena cava obstruction, and hepatic vein obstruction (e.g. Budd-Chiari syndrome). The second mechanism is decreased oncotic pressure due to hypoalbuminemia, which can be caused by nephrotic syndrome, protein losing enteropathy, severe malnutrition, as well as cirrhosis again. Thirdly, when the fluid production exceeds the resorptive capacity of the peritoneum, ascites may develop, as in infections such as tuberculosis and filariasis, and malignancy. Finally, salt and water retention may occur as a consequence of increased aldosterone production, as well as other hormonal mechanisms.[3]

In alcohol abusers, cirrhosis is the most likely cause of ascites, but other causes such as malignant ascites from hepatocellular carcinoma, heart failure, acute pancreatitis, and tuberculosis should be considered. We should now hear more about this man's abdominal pain.

P: Two days prior to presentation, this man began complaining of band like pain around the whole abdomen. This pain was mild, constant, and not relieved by food, passing gas or a bowel movement.

Dr. S: The new onset of pain in this gentleman is disturbing. If we use the principle of Occam's razor, which, as it applies to medicine, suggests that all symptoms may be appropriately explained by one diagnosis, we must attempt to tie together all the facts in this case to arrive at a single unifying cause. According to this logic, we have two possible hypotheses: malignancy or ascites. If the patient's swelling is due to a tumour, the pain is easily explained by the tumour itself. If the patient has ascites, the pain may be due to stretching of skin and subcutaneous tissue, or may be the result of spontaneous bacterial peritonitis (SBP), an infection of the abdominal peritoneum. Ascitic fluid is a filtrate of serum, but is lacking in opsonins and immunoglobulins and therefore has a decreased ability to aid the immune system in resisting infection. Thus, ascites is an excellent culture medium. Patients with ascites are at risk for developing bacterial peritonitis, in the absence of a secondary cause such as a bowel perforation. The pathogenesis is incompletely understood, but it is suggested that luminal organisms traverse the bowel serosal surface and lead to peritonitis, thereby causing abdominal pain. SBP is a serious condition, and it heralds a poor prognosis, with a mortality rate between 40% and 60%. Typical symptoms are fever and abdominal pain in the setting of a patient with known ascites. Other symptoms can include encephalopathy and generalized deterioration, but many patients are asymptomatic.[4,5] Other common causes of abdominal pain in alcohol users should also be considered, including peptic ulcer disease, gastritis, and hepatitis. We should now proceed to the physical examination.

P: What should be the focus of the physical examination?

Dr. S: The first focus should always be the vital status of the patient - the "ABC's." Airway is not an issue here. Breathing should be assessed by respiratory rate, accessory muscle use, chest examination, and an assessment of oxygen saturation via pulse oximetry. Circulation should be assessed by the measurement of the pulse, blood pressure and an assessment of peripheral perfusion. Temperature should be noted.

The next focus should be on the abdomen. The diagnostic dilemma of this case is whether the patient has ascites as the cause of the abdominal swelling. There are several techniques for eliciting this information. If ascites is present, on inspection, the abdomen will be protuberant, with bulging flanks. In severe ascites, the umbilicus will evert, giving the patient an impressive "outie." There may be dilated surface veins on the abdomen, and around the umbilicus (caput medusae), signifying the presence of portal hypertension. On percussion of the abdomen, a pattern of periumbilical tympany may be surrounded by flank dullness, due to gas filled loops of bowel floating on a sea of ascites. Two maneuvers are traditionally used to elicit ascites, shifting dullness and fluid wave. Shifting dullness is performed by percussing the abdomen laterally from the umbilicus, in order to find the level at which the ascites begins. When the percussion note changes from tympany to dullness, a mark is made. The patient is then instructed to lean away from the examiner. The abdomen is repercussed. As ascites is usually free flowing, the fluid will swing laterally, causing the change in the percussion note from tympany to dullness to shift towards the examiner, and the test to be positive for shifting dullness. A fluid wave is demonstrated by having the patient or an assistant vertically compress the abdomen in the midline. One hand is placed on one flank, and the other hand flicks the other flank, in order to create a wave in the ascitic fluid. As the wave swings across the abdomen, it will be palpable with the sensing hand over the opposite flank. A third maneuver in the literature, the "puddle" sign, involves having the patient kneel on all fours, while the examiner attempts to elicit periumbilical dullness by percussion. This maneuver is undignified and demeaning to the patient, and should never be performed.[6]

P: How good are these maneuvers in the detection of ascites?

Dr. S: The absence of bulging flanks, flank dullness, or shifting dullness has a sensitivity of approximately 80% for ruling out ascites, but are less specific, approximately 70%. The presence of a fluid wave has a specificity of 90% for ruling in ascites. Interestingly, the absence of ankle swelling on history has the highest sensitivity of all, at 93%.[6]

Once ascites has been suggested on physical examination, a more detailed abdominal examination should be performed, and should assess the patient for focal tenderness, masses, rectal masses, hepatosplenomegaly, and the stigmata of chronic liver disease (see Table 1). A cardiac examination should focus on evaluation for right heart failure. Special attention should be given to the assessment of the JVP, which may be quite elevated in certain conditions such as constrictive pericarditis or severe right heart failure and therefore be missed on a casual inspection. A general examination should be performed, focusing on diagnostic possibilities from our list of possible causes for ascites.

Table 1
Physical Signs of Cirrhosis

Physical sign	Presumed mechanism
Jaundice	Liver decompensation
Temporalis muscle atrophy	Malnutrition
Parotid gland swelling	Unclear (usually associated with alcoholism)
Spider angiomata	Increased circulating estrogen due to inadequate hepatic metabolism of androstenedione
Testicular atrophy	"
Gynecomastia	"
Loss of axillary/pubic hair	"
Palmar erythema	"
Clubbing	Unknown
Ascites	Portal hypertension
Caput Medusea (periumbilical veins)	"
Dilated abdominal veins	"
Hemorrhoids	"
Splenomegaly	"
Ecchymoses	Decreased hepatic production of clotting factors

Other physical findings may be seen in specialized etiologies of cirrhosis, such as hemochromatosis and primary biliary cirrhosis.

P: On examination, the patient appeared unwell, with obvious abdominal distension. Vital signs were normal, the patient was afebrile, and no postural drop in blood pressure was noted. Head and neck examination was normal. The chest was clear to auscultation and percussion. Cardiovascular examination revealed a JVP at 1 cm above the sternal angle. The precordial examination was normal, with normal heart sounds, no extra sounds or murmurs. Abdominal examination revealed a distended abdomen with bulging flanks. There were dilated surface veins present on the upper part of the abdomen. The umbilicus was everted. Both shifting dullness and a fluid wave were present. The liver measured 8 cm in the midclavicular line, and was not palpable. There was a positive splenic percussion sign, and the spleen was palpable in the left upper quadrant. The abdomen was diffusely tender to percussion and palpation, but no rebound or guarding was noted. Palmar erythema, testicular atrophy, and gynecomastia were noted. There was a small amount of pitting edema present at the ankles, but no sacral edema was noted. The neurological and musculoskeletal examinations were normal.

Dr. S: The physical examination confirms our suspicion for ascites, and strongly suggests cirrhosis with portal hypertension. This suspicion is based on the findings of dilated surface veins on the abdomen, and the presence of ascites and splenomegaly, all of which are caused by portal hypertension. Cardiac causes of ascites, such as CHF and constrictive pericarditis are much less likely given the low JVP. Nephrotic syndrome, infection, and malignancy can only be ruled out through further testing. The question now is what caused the cirrhotic decompensation leading to ascites in this patient – SBP, alcoholic hepatitis, hepatocellular carcinoma, or superimposed cardiac or renal disease?

P: What investigations would you order for this patient?

Dr. S: Serologic testing should include routine blood work, such as a CBC, electrolytes, and renal function (BUN and creatinine). Liver enzymes (AST, ALT, ALP, GGT), and liver function tests, such as albumin and INR/PTT should be ordered. As well, testing for other causes of liver disease should be done at this time, including hepatitis B and C serology, ceruloplasmin for Wilson's disease, iron saturation for hemochromatosis, and α1-anti-trypsin for α1-anti-trypsin deficiency. A serum αfetoprotein should be ordered for the investigation of hepatocellular carcinoma, as it is elevated in this condition. An ultrasound of the abdomen should be performed at some time to assess the size of the liver, the presence of ascites, and the possible presence of an underlying liver malignancy. In this patient, the most important investigation however, will be to sample the fluid in the abdomen - a diagnostic paracentesis. This can aid in the diagnosis of portal hypertension, infection, and malignancy.

P: When is a paracentesis performed? How is it performed? What are the contraindications?

Dr. S: Paracentesis should be performed in all patients with new onset ascites at the time of presentation, whenever there is a clinical suspicion for infection, and for symptoms of abdominal swelling due to a high volume of fluid. It is an easy and safe procedure to perform, and has no absolute contraindications. Even in patients with a coagulopathy, the procedure is safe and causes little blood loss. It is performed in the left lower flank, to avoid vascular structures and intraperitoneal viscera. Approximately 30 to 100 cc's of fluid are removed for diagnostic testing.

P: How does the ascitic fluid analysis aid in the diagnosis of this patient?

Dr. S: The fluid should be sent for cell count and differential, Gram stain and culture, culture for mycobacteria, albumin, and cytology. The serum-ascites albumin gradient can distinguish ascites due to portal hypertension from that not due to portal hypertension in the overwhelming majority of cases. This gradient is simply the serum albumin concentration minus the ascitic fluid albumin concentration. Values greater that 11g/L predict ascites due to increased portal pressure. This would help eliminate tuberculous and malignant ascites from the differential diagnosis.[7,8]

The cell count in the fluid is a crucial piece of information for the diagnosis of SBP. A neutrophil count greater

than 250 cells/mm^3 strongly suggests the diagnosis. A Gram stain would also be helpful; however, it is not always readily available. Although some senior clinicians bemoan the loss of the ability to perform a Gram stain by our current generation of housestaff, I feel that this technique is best left to those who perform it for a living.

P: Laboratory investigations and paracentesis results are shown in Table 2.

Table 2
Laboratory Findings

Tests	Result	Range
Hemoglobin (g/L)	120	140-160
White cell count (per mm^3)	12.0	4-11
Platelet count (per mm^3)	110	140-150
Electrolytes (meq/L)	Sodium 130, all others normal	136-146
Creatinine (mmol/L)	110	<133
AST (IU/L)	65	<38
ALT (IU/L)	45	<38
ALP (IU/L)	200	
Total bilirubin (mmol/L)	25	<20
INR	1.4	0.88-1.1
PTT (sec)	40	23.5-32.5
Albumin (g/L)	25	37-48
Paracentesis: Neutrophil count (per mm^3)	500 cells	
Paracentesis: Albumin (g/L)	5	

**all other test results normal*

Dr. S: There is mild elevation of the AST and ALT, suggesting ongoing hepatocellular necrosis from mild alcoholic hepatitis, and the ALP is doubled above the upper limit of normal, suggesting cholestasis. These results, together with the other investigations, history and physical examination, suggest this gentleman likely has cirrhosis. The serum sodium is mildly depressed, due to water retention from aldosterone and possibly ADH secretion in response to a decreased extracellular volume. The mild anemia and thrombocytopenia is likely on the basis of splenomegaly and subsequent sequestration, although an acute toxic effect of alcohol on bone marrow production cannot be excluded. The serum-ascites albumin gradient is 20 g/L, strongly increasing the likelihood of portal hypertension as the etiology of the ascites. The ascitic fluid neutrophil count is high, suggesting SBP. I would now proceed to treatment of this patient.

The first issue is the SBP. SBP is a reversible cause of morbidity and mortality and treatment should be started immediately. Initially, one does not have culture or Gram stain results to guide therapy; therefore, empiric broad spectrum antibiotics to cover relevant organisms should be initiated. The common causes include *E. Coli, Enterococcus* species, and *Klebsiella pneumoniae,* accounting for over 86% of cases. Other organisms include other gram negative bacilli, and rarely anaerobes and staphylococci. Usual coverage is with a third generation cephalosporin such as cefotaxime. Other alternatives include ampicillin and clavulinic acid, or ampicillin combined with a quinolone antibiotic. Aminoglycosides should be avoided due to potential nephrotoxicity. The antibiotic choice can be tailored once culture and sensitivity results are available.[4,5]

The second issue is the management of ascites. The goal of therapy is comfort and preventing complications. Ascites is disfiguring, tiring, and can be painful. It can restrict mobility, decrease appetite, and cause early satiety. It also increases the likelihood of the development of hepatorenal syndrome, a condition of progressive renal insufficiency that is invariably fatal. It may also increase the risk of esophageal variceal bleeding due to acid reflux into the esophagus from increased intra-abdominal pressure. Therapy aims to control the volume of fluid. Initial measures are conservative in nature. These include bed rest, salt restriction and diuretic therapy, usually with a potassium sparing diuretic such as spironolactone or amiloride. These drugs act as aldosterone antagonists, although by different mechanisms. There is little to choose between the two, but spironolactone has the side effect of painful gynecomastia, which may already be a problem in a patient with cirrhosis.

If these measures are ineffective, invasive methods can be used. Total volume paracentesis uses repeated abdominal taps to drain the abdomen of fluid. It is indicated when patients have recurrent high volume ascites that causes symptoms. When the volume of fluid removed is greater than 5 L, intravenous albumin is given to prevent intravascular volume depletion. If this method is unsuccessful, insertion of a porto-systemic shunt is an option. It allows portal blood to bypass the liver, thus decreasing portal pressure and eliminating one of the mechanisms of ascites formation. The most popular shunt these days is a trans-jugular intrahepatic porto-systemic shunt (TIPS). It is inserted by an interventional radiologist via the internal jugular vein, and a shunt is created in the liver between the portal and venous systems. It has the added effect of decreasing the risk of bleeding from esophageal varices. However, it has some risks, including bleeding from the actual procedure itself, and encephalopathy.[9,10]

The third issue is the management of cirrhosis. The goals of therapy are to reduce ongoing liver damage and prevent complications. The most important therapy in this man will be alcohol cessation. This will have the most impact on his future survival. Adequate nutrition should be given, and multivitamins, especially thiamine, should be prescribed. Consideration should be given to endoscopy to determine the presence of esophageal varices, as treatment with ß-blockers has been shown to reduce first bleeding from varices that have the endoscopic appearance of high-risk lesions.[11] The role of liver biopsy in this

disease is controversial. The main reason to do this procedure would be to rule out other non-alcoholic causes of cirrhosis, and I would refer this gentleman to a gastroenterologist for further consideration of this procedure.

P: The patient was admitted to hospital, started on bed rest, salt restriction, furosemide, spironolactone, and antibiotics. Total volume paracentesis was successful in removing 11 L of fluid. Endoscopy revealed several varices considered high risk, and nadolol, a ß-blocker, was started. He was discharged 7 days after admission, with no re-accumulation of his ascites. An appointment was made at the Addiction Research Foundation for alcohol cessation counselling. What were the reasons for hospitalization of this patient versus an outpatient management?

Dr. S: We identified the cause of the ascites, namely cirrhosis. He needed inpatient management of his SBP, namely intravenous antibiotics. We initiated diuretic therapy and were able to monitor his electrolytes and renal function. Lastly, an intervention such as this may be what it takes to get this gentlemen to stop drinking. A brush with death tends to change patient behaviour.

P: What is this patient's prognosis?

Dr. S: Not great. There is a 70% recurrence of SBP in the first year. As well, patients with cirrhosis and ascites have a 50% two year mortality.[4,5] However, this may be improved with alcohol cessation.

This case illustrates the value of an appropriately directed history and clinical examination. The case hinges on the ability of the clinician to diagnose ascites. On history, we were able to explore the history of alcohol use. Using good physical examination technique, we were fairly confident of the diagnosis, and proceeded to paracentesis without ultrasound confirmation of the presence of fluid. To paraphrase Ira Gershwin, if the fluid doesn't swing, it don't mean a thing.

CLINICAL PEARLS

- The differential diagnosis of the patient with a swollen abdomen is best remembered using a physiologic framework. Think "solid", "liquid", and "gas."
- Physical examination maneuvers with the highest sensitivity for ascites are bulging flanks, peripheral edema, and shifting dullness. Their absence tends to rule out ascites. A positive fluid wave has a high specificity for ascites and its presence tends to rule in ascites.
- A diagnostic paracentesis should be performed on all patients with newly diagnosed ascites. It is useful in the diagnosis of SBP, and can rule in portal hypertension as the cause of ascites.
- SBP is a treatable complication of ascites and has a one year mortality approaching 40%.

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The Last 25 Years

Kurt Droll, MSc. (OTO) and Ryan Foster, BSc. (OTO)

In December of 1923, the University of Toronto Medical Journal *(UTMJ)* published its first issue and began its chronicle of the ever-changing face of medicine at the University of Toronto. *From the Archives* showcases some of the most memorable and insightful research, editorials, and photographs previously published in the *UTMJ*. The first issue from Volume 75 displayed highlights from the first 25 years (1923-1948) while the second issue explored the *UTMJ* over the middle 25 years (1948-1973). In this final issue from the 75th volume, we present the closing installment of *From the Archives* with a look at **The Last 25 Years** (1973-1998).

The Beginnings of a Pandemic

The Acquired Immune Deficiency Syndrome *(AIDS)* is the most tragic disease to command our attention in the last 25 years. The *UTMJ* recorded the scourge of this diseaes since it first appeared in the medical literature. Below we present an excerpt from the first documentations of AIDS in the *UTMJ*, Volume 61, Number 1 in October 1983.

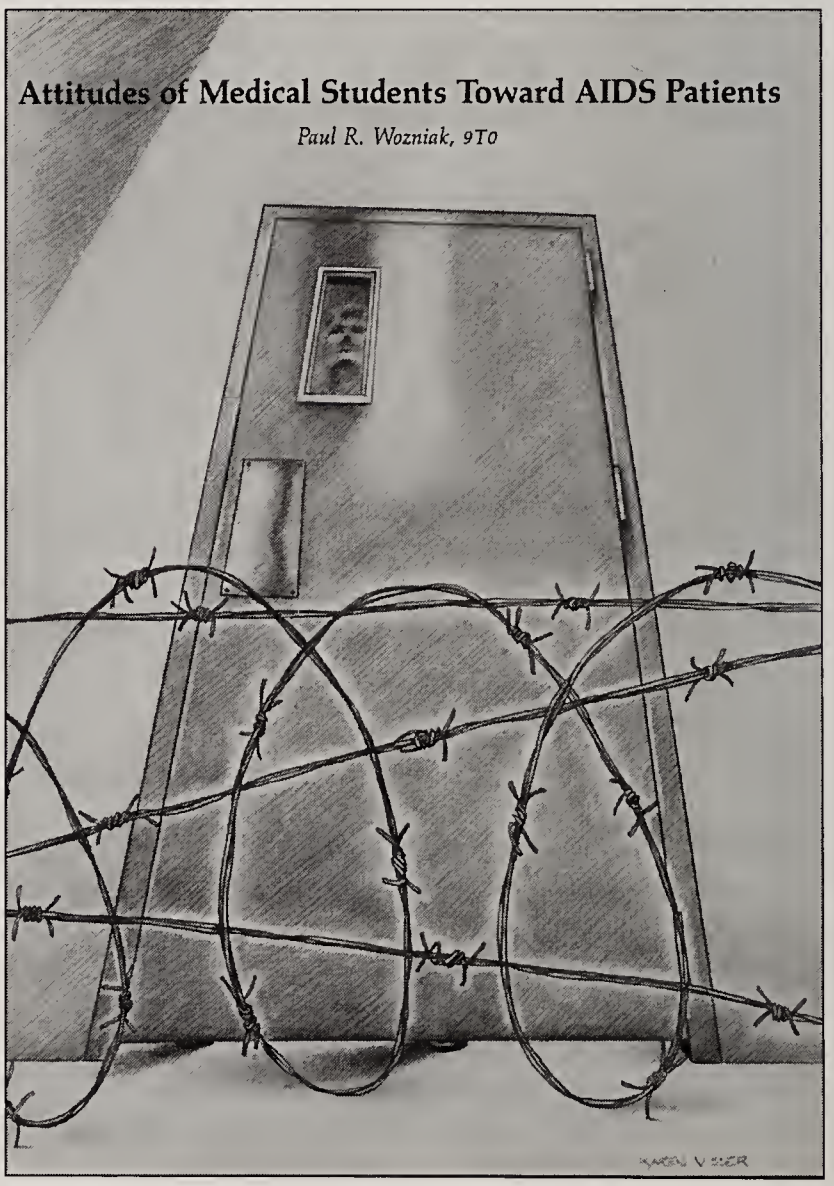
In Canada, the first documented case occurred in Windsor in January, 1982 and since then over 49 cases have been reported to the LCDC in Ottawa. In contrast to the American experience, 28% of Canadian cases have occurred in recent Haitian immigrants, mainly in the province of Quebec. A comparison of the Canadian and American subgroups is shown in Table 2. Twenty-nine of the Canadian cases have died yielding a case fatality rate of 59% at two years.[1]

Table 2. — Percentage Distribution of Cases, by Risk Group — Canada versus U.S.A.

Risk Group	Canada %	U.S.A. %
Homosexual/Bisexual Males	46.0	75.0
Intravenous Drug Abusers	2.0	13.0
Haitians	28.0	6.0
Hemophiliacs	4.0	1.0
Other	20.0	5.0
	100.0	100.0

Graphic Horror

AIDS has always evoked powerful images and emotions in us all. This drawing, published in April 1988, depicts in haunting fashion, attitudes that many in the medical community initially expressed towards AIDS patients.



Breaking New Ground

During the last 25 years, there have been several major research accomplishments reported by clinicians and researchers at the University of Toronto. The *UTMJ* has provided a forum for the reporting and discussion of these significant achievements. Here is a snap-shot of some groundbreaking research during this time.

Molecules of the Mind

Dr. Phil Seemen has played, and continues to play, a significant role in unlocking the molecular mysteries of the human brain. His work with various neurotransmitter systems has led to his advanced definition of the Dopaminergic System, and its effects on behaviour. The following excerpt is from an article by Dr. Seemen which appeared in Volume 52, January 1975.

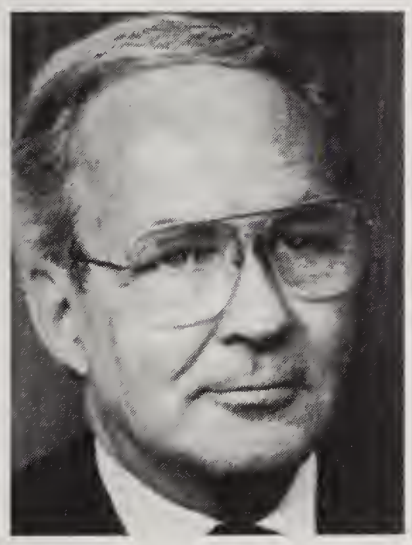
In addition to glutamate, there are now thought to be about a dozen neurotransmitters in the brain, and one of these is 5-hydroxytryptamine (5-HT). Normal levels of this transmitter appear to be essential for sleep, and probably for normal mood processes, although direct proof for this latter function is still lacking. There is considerable research attempting to stimulate 5-HT synthesis in the brain.

One of the current important discoveries in medicine is that of membrane receptor diseases. Membrane receptors for the neurotransmitters, as well as receptors for steroids, for convulsants and tranquilizers, and for hormones are being discovered, isolated and purified. This will open up a whole new chapter in the diagnosis of various diseases.

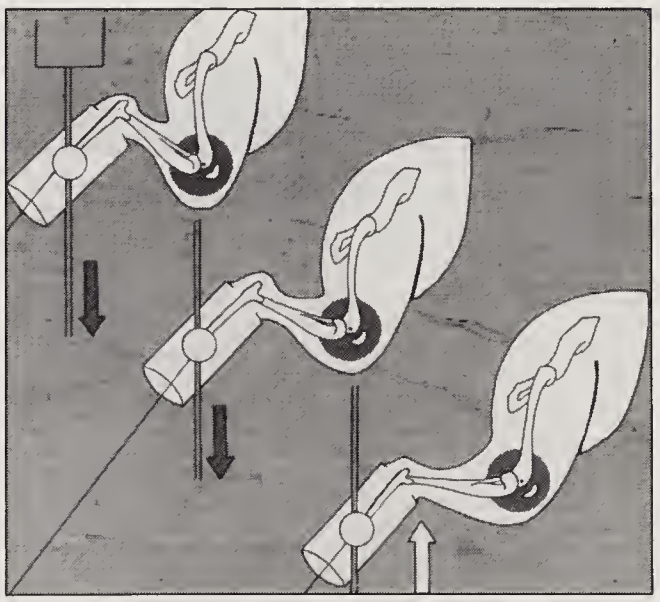
The ultimate goal is not only to prevent and cure disease, but to understand human behaviour as well, if this is possible. It could be, for example, that people tend to choose the right-hand staircase (or keep to the right) because the dopamine content in the contralateral striatum is slightly higher than that in the ipsilateral side; certainly this is the case in rats[3]. But human behaviour must be more complicated than this and it will probably take many hundreds of years before a clear picture of brain function emerges.

Movin', Groovin' and Soothin'

Dr. Robert Salter of the University of Toronto is a world-renowned orthopedic surgeon who is best known for Continous Passive Motion (CPM); a revolutionary concept promoting continuous motion of a limb post-operatively. At the time it debunked the long held practice of post-operative limb immobilization. Here we present a portion of an interview previously published in 1994, Volume 71, Number 3.



When asked whether he has ever found it hard to challenge pre-existing ideas, Dr. Salter exclaims that for some of his original ideas he has faced considerable skepticism. One idea in particular was that of continuous passive motion. He originally conceived the idea from many observations including his own experiences as an athlete and the many injuries he sustained while at the University of Toronto. "I learned if I could stay away from an orthopaedic surgeon and not be put in a cast, I then did a lot better." Many of his teachers disagreed with this notion, their defence being that "...for centuries the medical profession has immobilized injured joints and surely not everyone is wrong." But Dr. Salter refused to accept this and in 1970 he began working on CPM. To date all the studies have demonstrated the greater efficacy of this technique compared with immobilization.



This figure illustrates some of the early rabbit model experiments which tested the CPM hypothesis. CPM was incorporated into medical practice in the late 1970s to improve post-operative conditioning, and today continues to be a useful method of rehabilitation.

Inspirational Icons

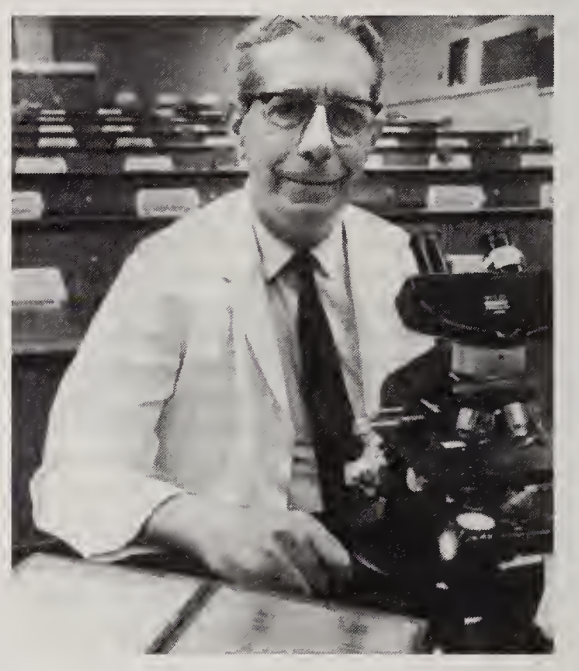
The University of Toronto has provided many students with role models who have had a profound influence on us, shaping our professional and personal development. We would like to honour two special role models who have helped students down the noble path of medicine; Dr. Robert Murrary and the late Prof. Harry Whittaker. Their resolute commitment to medical students has been inspirational.

Murray's Triad: Haggis, Humour and Holoenzymes

In March of 1998, amidst a packed lecture auditorium of kilted students, teary-eyed colleagues, and bagpipes, Dr. Robert Murray delivered his last lecture at the University of Toronto Medical School. His reign had lasted four decades, and as he proclaimed "one of my students is now one of the deans," we all began to realize the true impact he has had at this medical school. In particular, Dr. Murray holds a special place in our *UTMJ* hearts, not only due to his undying support of the journal, but also because of the creation of the Medical Student Research Day here at University of Toronto.He, along with Dr. Niall Byrne, started this Research Day in 1987. Since then, the *UTMJ* has published a supplement of the proceedings of the Student Research Day. This research is often the backbone for many *UTMJ* submissions. Below is a photograph of Dr. Murray that appeared in Volume 65, Supplement 1, in September 1988. It is fitting that in this commemorative section we are able to say so long – but certainly not good-bye – to the much loved, appreciated and soon to be dearly missed Dr. Murray, whose sense of humour, dedication to students and *joie de vivre* will make him one of U of T's all time greats. We wish Dr. Murray all the best in his retirement. Go Scotland!

Prof. Harry Whittaker

If anyone ever ruled the medical school, it was the late Harry Whittaker. Prof. Whittaker passed away in 1985, and although the current *UTMJ* staff is not personally familiar with him (aside from the many tales of this man's kindness), it is well known that many classes before us were graced with his dedication and leadership. For over 50 years, Harry Whittaker made his students "keep things simple" in the Histology Lab. In his memory, we present a small clip of his **In Memoriam,** written by an 8T5 graduating student, from Volume 63, Number 1, in December of 1985.



"Did you know Harry?' I asked. 'Of course' he replied. 'Everyone who went through U of T knew Harry. You know, I bumped into him a few months ago and he knew who I was and called me by name! That's quite remarkable considering I graduate over ten years ago with 249 other students. I wasn't exactly conspicuous in the histology class either,' he added.

To the 1st-year medical students and many 1st-year classes to come, Histology will be different. Trying to picture Histology without Harry is, for me, like trying to visualize a portrait without a background. Yes, Histology will survive. It just won't be the same. It's like growing up with your grandfather and going home from school one day to learn he's no longer there.

As for those of us who were privileged to know Harry, the memories will always linger on. The gentle smile. The constant reassurances that — yes, you *will* pass histology. And yes — *you* will become a doctor. Harry added that special warmth to the spirit of comraderie in Canada's largest Medical School which we will never forget. On my own behalf, and on behalf of all my colleagues who have graduated over the years — especially on behalf of the class if 8T5 — I say, 'Thanks, Harry!'

A Student's Vision

As a final tribute to the last 75 years, this installment of *From the Archives* closes with an editorial that appeared in Volume 52, Number 4 in February of 1975. With great interest, we now reprint the fascinating details describing the inception of the *Journal* some 75 years ago.

The Origin of the University of Toronto Medical Journal

Earlier this year it was our good fortune to receive from Dr. Benjamin I. Johnstone (2T4) a short letter on the initiation of the Medical Journal. We would like to share the letter with you.

" . . . After half a century, I thought you might be interested in learning about the birth of this publication. In 1922 Don Campbell of 2T3 was a candidate for presidency of the Medical Society. One of his platform planks was the establishment of an undergraduate Medical Journal. Don was elected president but, for some reason, he did not carry out his plan. The next year – in 1923 – I ran for the presidency and promised to start the Journal, if possible. I was elected president and Jerry Campbell of 2T6 was elected secretary-treasurer.

My first problem was to obtain permission from the faculty. I met with this group consisting of the Dean, Professor Duncan Graham, Professor J. J. R. McLeod, Professor F. W. G. Starr, Professor V. Henderson, and others. They agreed we might go ahead but with two very strict provisos:

1. The word "undergraduate" must be displayed prominently on the front page of the Journal.
2. They would assume no financial responsibility for the undertaking.

Having obtained permission, the next problem was to learn where a Journal could be published. I contacted Mr. Brebner, the registrar, and after some consideration he agreed to publish the Journal provided we were able to guarantee payment.

During the summer of 1923, Jerry Campbell and I visited Eatons, Simpsons, various surgical supply houses, and others whom we thought might be interested in advertising in such a Journal. By the end of the summer, we had obtained sufficient guaranteed advertisements to cover the cost and Mr. Brebner agreed to go ahead with the publication.

Early in the school year, the first issue was published. The executive committee of each of the five years undertook to sell each of their members a copy at ten cents each. The venture did not turn out to be a big money maker but, fortunately, we ended up in the black.

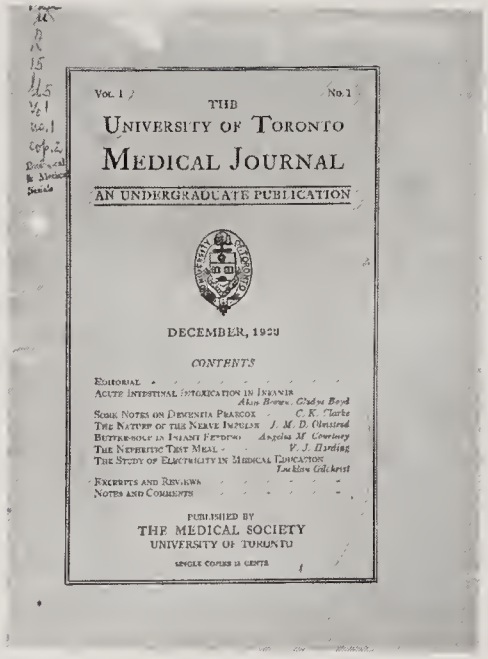
The Medical Society appointed Earle Scarlett, 2T4, as Editor-In-Chief and he selected members from each of the years for his committee. The literary success of the Journal was entirely due to Earle Scarlett and his editorial board . . . "

After 52 consecutive years of publication the Journal remains one of the oldest undergraduate medical publications on the continent.

Final Words

As the final issue of the 75th year comes to a close, *From the Archives* reflects upon its 75 year history. During the course of its publication, the *UTMJ* has seen the development and world wide implementation of insulin, and the construction of Canada's first hospital dedicated to women. It has had the privilege to be associated with a multitude of great clinician scientists and a two time Nobel Laureate.

As we have shown, the *Journal* has witnessed tumultuous times; but the commitment and vision of the editors, authors, and generous support from patrons has sustained this student-directed publication. We salute the last 75 years, and to the next 75, we wish you all the best. For our final piece of nostalgia, we present a two page layout of the major design changes of the *UTMJ* over the past 75 years.



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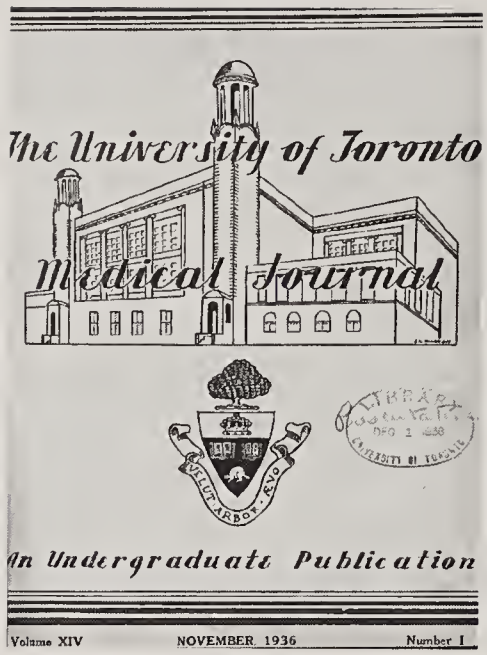
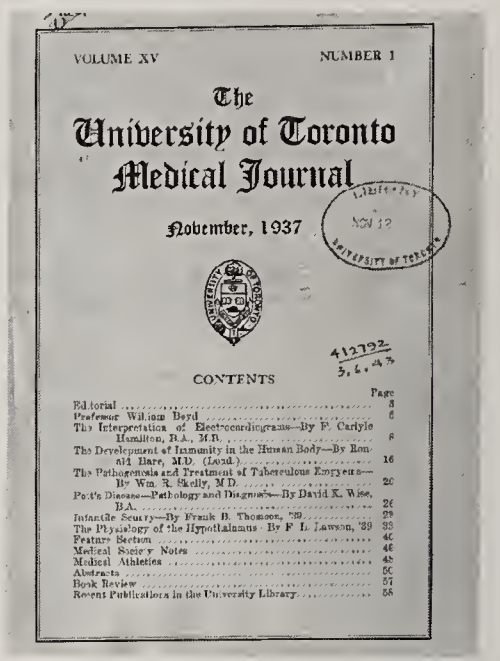


Volume 14, No. 1, 1936



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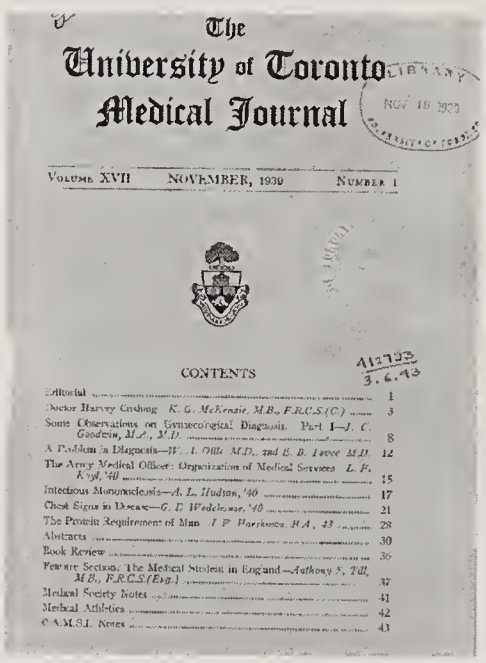
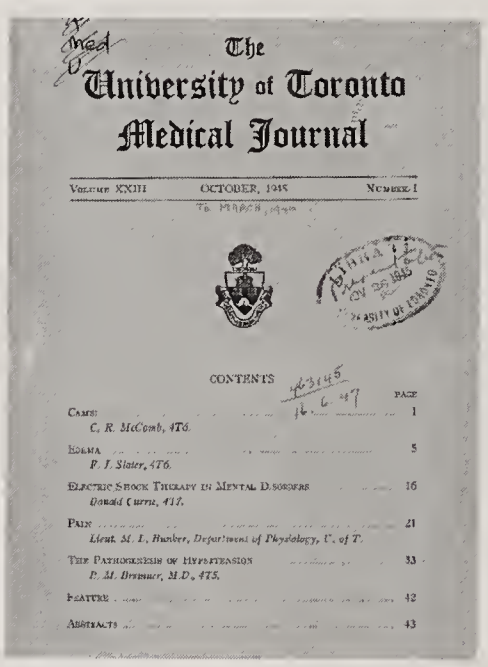


Volume 17, No. 1, 1939



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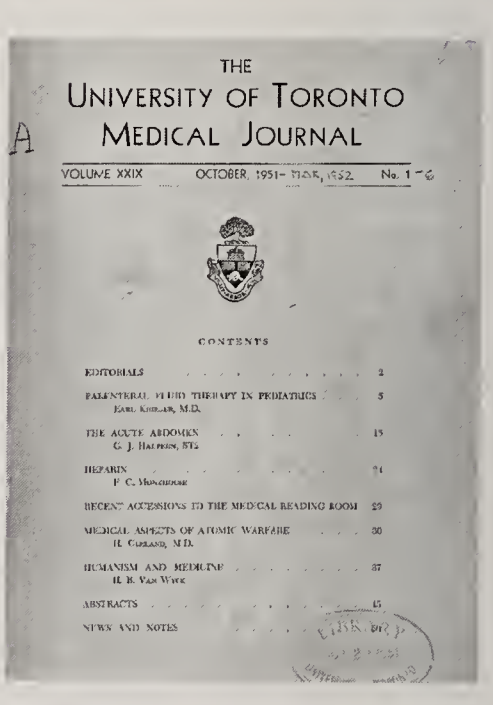

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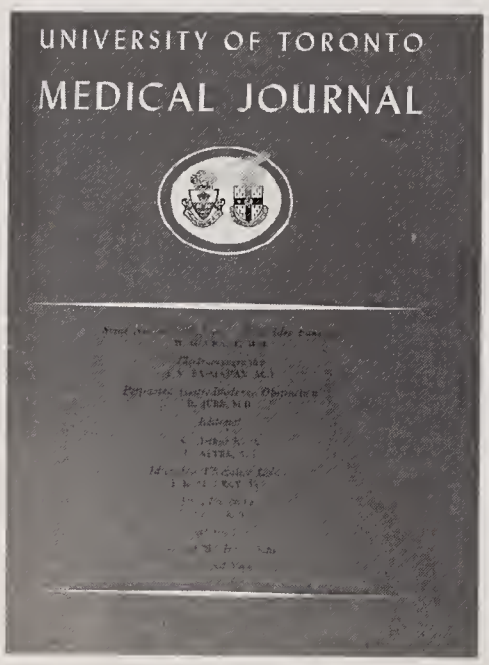

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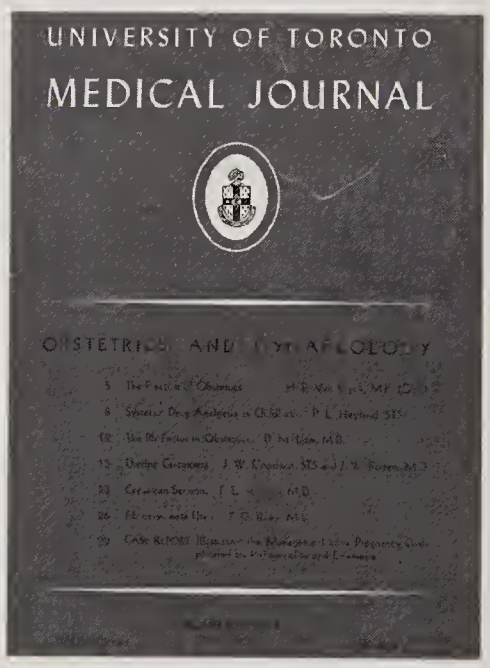

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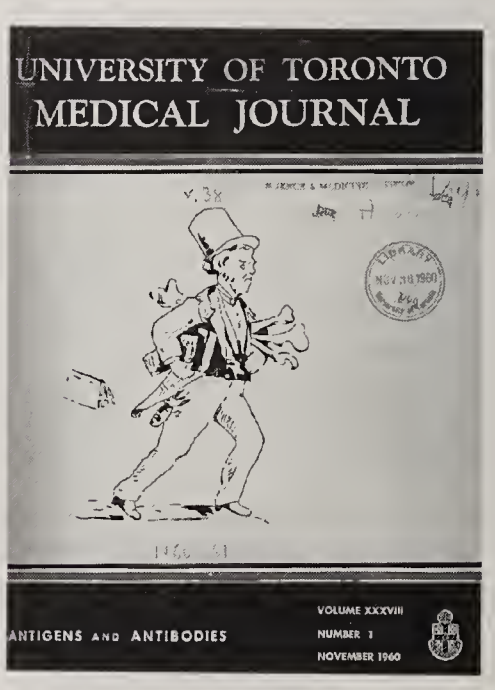
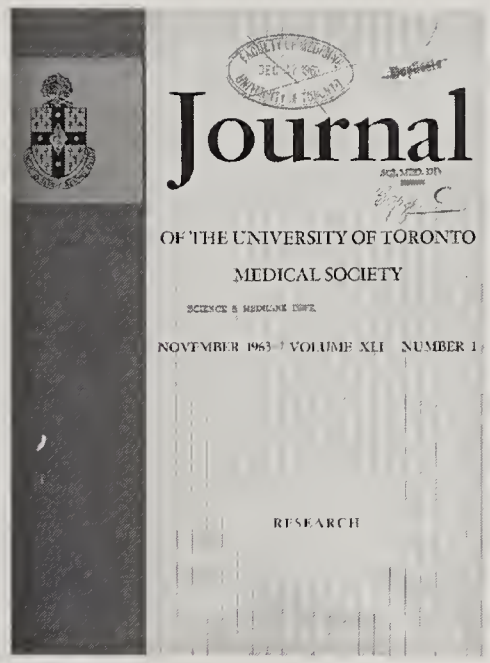


Volume 38, No. 1, 1960



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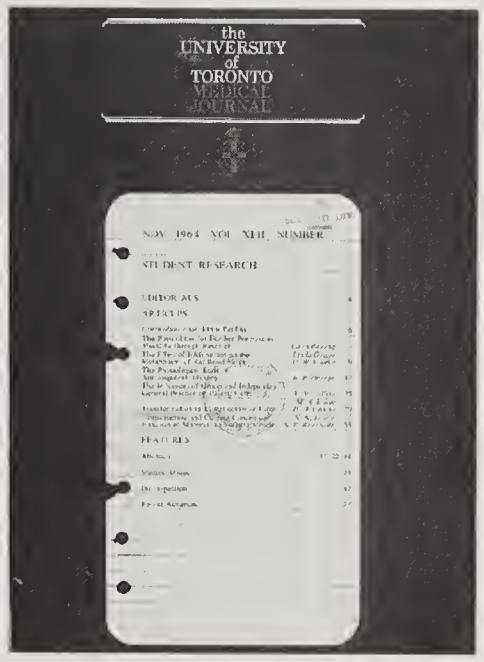

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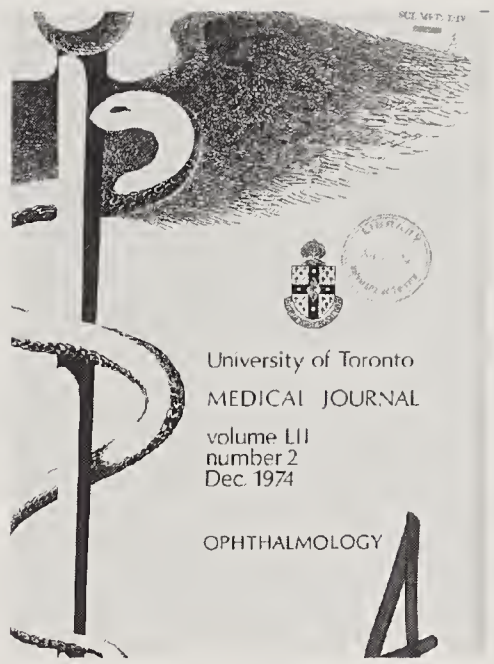

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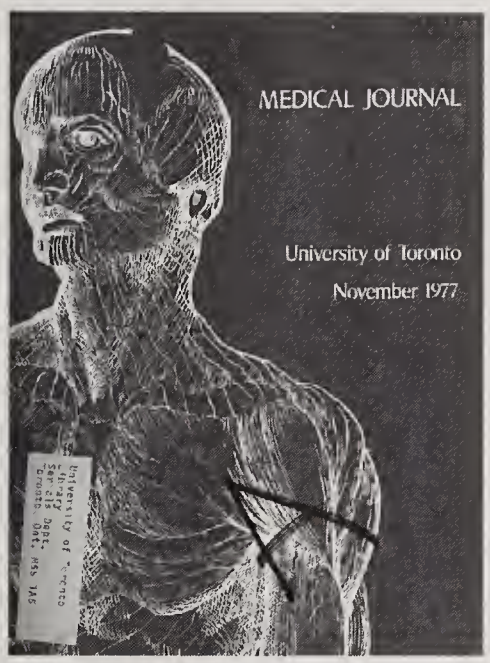

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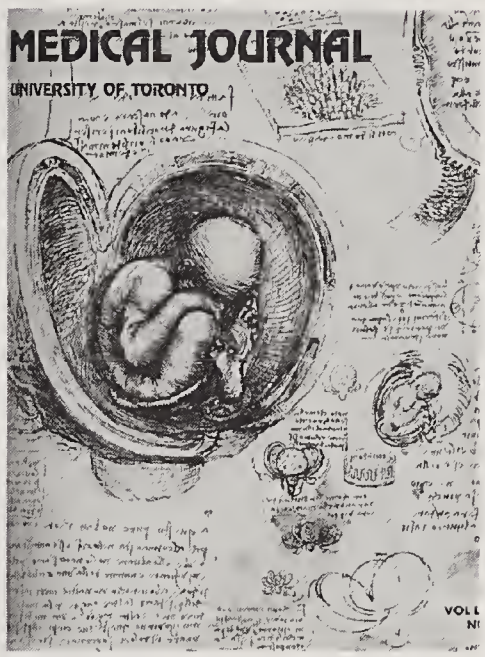
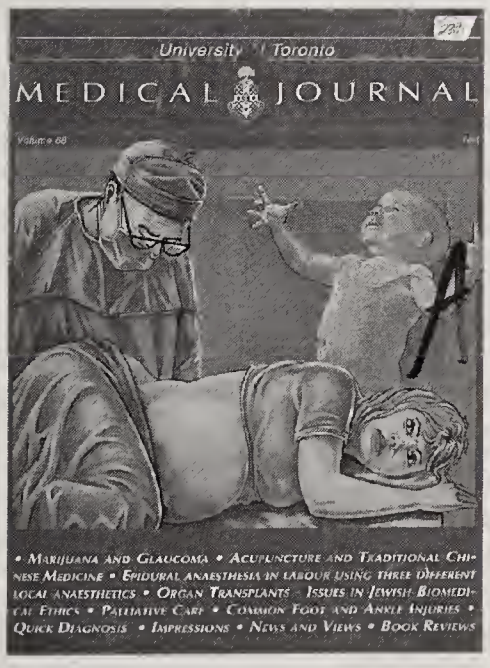
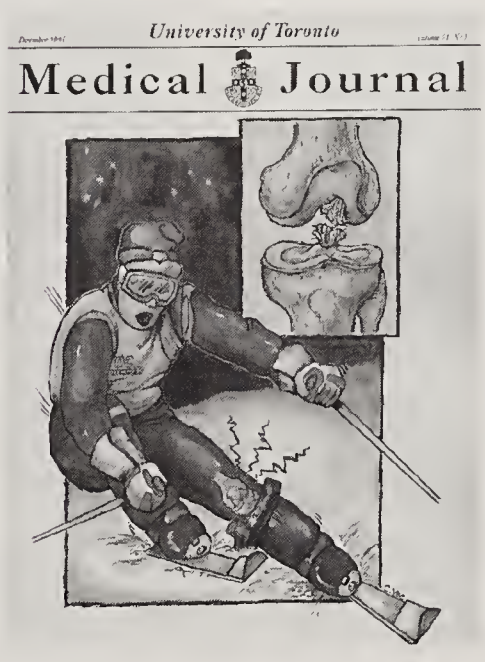


Volume 57, No. 1, 1979

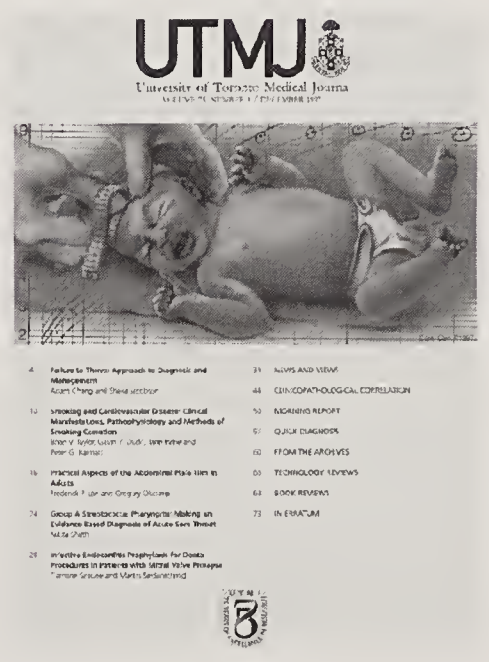
Volume 60, No. 1, 1982


University of Toronto
MEDICAL JOURNAL
• Marijuana and Glaucoma • Acupuncture and Traditional Chinese Medicine • Epidural anaesthesia in labour using three different local anaesthetics • Organ Transplants - Issues in Jewish Biomedical Ethics • Palliative Care • Common Foot and Ankle Injuries • Quick Diagnosis • Impressions • News and Views • Book Reviews

Volume 68, No. 1, 1990



Volume 71, No. 1, 1993

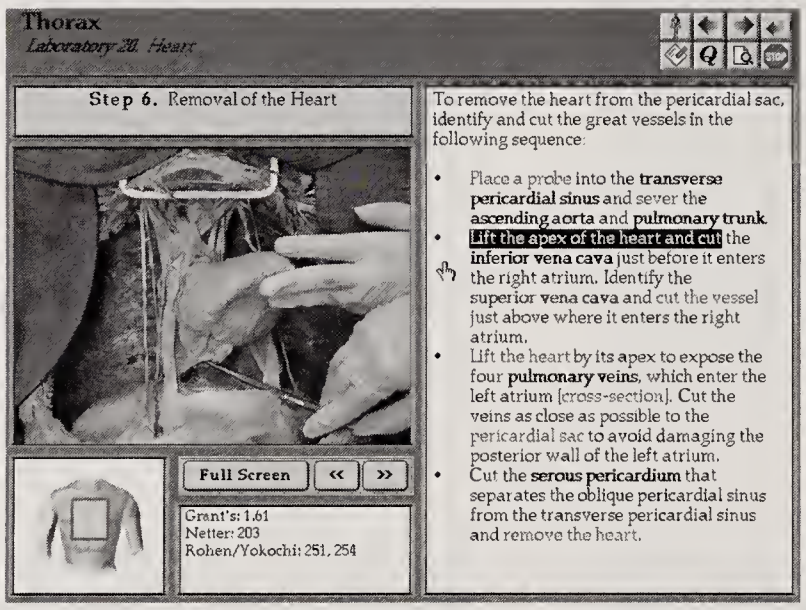


Volume 75, No. 1, 1997

Human Anatomy on CD-ROM

Dan Perri, BScPhm., (OTO)

Human Anatomy was created by a team of anatomy professors from the College of Medicine at the University of Florida. It's intent was to combine the text of a dissection manual with photographs of dissected specimens similar to those in an anatomy text. The CD contains a gallery of 6000 images and illustrations that complement the step-by-step dissection instructions. Add to this over 4700 practical exam questions and the package becomes a powerful anatomy teaching and studying tool.


Thorax
Laboratory 20. Heart
Step 6. Removal of the Heart
To remove the heart from the pericardial sac, identify and cut the great vessels in the following sequence:
Place a probe into the transverse pericardial sinus and sever the ascending aorta and pulmonary trunk.
Lift the apex of the heart and cut the inferior vena cava just before it enters the right atrium. Identify the superior vena cava and cut the vessel just above where it enters the right atrium.
Lift the heart by its apex to expose the four pulmonary veins, which enter the left atrium [cross-section]. Cut the veins as close as possible to the pericardial sac to avoid damaging the posterior wall of the left atrium.
Cut the serous pericardium that separates the oblique pericardial sinus from the transverse pericardial sinus and remove the heart.
Full Screen
Grant's: 1.61
Netter: 203
Rohen/Yokochi: 251, 254

The approach to dissection is of the typical regional gross anatomy type with tutorials divided into 44 "labs" covering seven regions including: back and spinal cord; upper extremity; lower extremity; thorax; head and neck; abdomen; and pelvis and perineum. It covers the cranial nerves and major neuroanatomy structures but does so quite superficially. The user can select the region of interest and may then choose specific laboratories which are targeted to specific organs or regions. Once a particular laboratory is chosen, the user may select one of four choices including: overview (objectives and list of photos); osteology (when appropriate); dissection procedure; or summary of terms (a review). An "orientation icon" on the screen helps the user to understand the position of the cadaver and the side of the body being examined (which is usually the right).

The quiz section of the program allows the user to define specific areas of questioning based on the seven anatomical regions or on osteology. Once a major region is selected, the user/student can even further divide the test questions into categories such as arteries and veins, bones, muscles, nerves, etc. so that detailed areas can be reviewed. Particularly useful in *Human Anatomy* is the cross-referencing of photographs to *Grant's Atlas of Anatomy* (9th ed.), *Netter's Atlas of Human Anatomy* (1st ed.), and *Rohen and Yokochi's Color Atlas of Anatomy* (3rd ed.) Another useful feature is the note pad which can be opened for study notes, which are automatically timed and dated and linked with the appropriate photograph, diagram, or screen location.

The software is similar for both Mac and PC with minor differences in the appearance of certain icons and with a "magnify" feature that is available on the Mac but not the PC version. The size of the window in the PC version depends on the video resolution, so if it is set high the pictures will not fill the whole screen. The high quality cadaveric photographs are best viewed in at least 16-bit colour. The downside to the CD is that it is not true multimedia in that photos are two-dimensional, pictures can not be "rotated," and it lacks the sound and animation found in other programs. Installation is straightforward but the CD is not equipped with an auto-run program so in Windows 95 it must be run using the program manager.

Overall, this is a powerful review and study tool which not only highlights key anatomical items but also outlines proper dissection technique. Gross anatomy students at all levels and in all disciplines will find it extremely helpful either before dissection or as a review.

C : \ Quick \ Reference \ Review
Gold Standard Multimedia Inc.
http://www.gsm.com
List Price: $99 (US)
Rating (out of 5):****

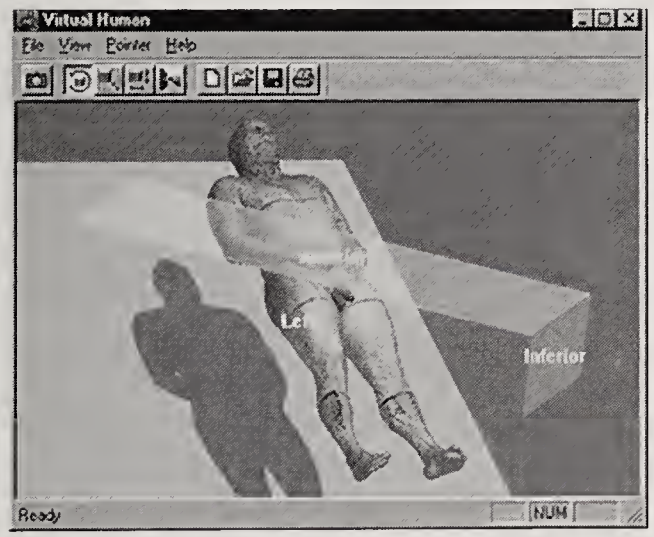
System Requirements:
Both PC and Mac are supported on the same CD
Windows - 486 or higher, Windows 3.1 or higher, 8MB RAM
Macintosh - System 7.0 or better, 68030 processor or better, 8MB RAM

Virtual Human CD-ROM Atlas

David Moskovitz, BSc. (OTO)

> In creating an atlas it is important to achieve a happy medium between complexity and simplification.
>
> *Frank H. Netter, MD*

The possibilities of multimedia technology as a teaching tool are becoming increasingly vast. *Virtual Human,* created by Spitzer, Whitlock and Seymour, contributes admirably to the field of educational computer software. The *Virtual Human* is a visualization application for graphically analyzing the human body. *Virtual Human* allows one to view three-dimensional images of bodily structures in an endless array of angles. The *Virtual Human* thrives in its ability to combine easy-to-use mouse driven commands with an expansive database of anatomical images. Moreover, the user can view an entire body or particular body part while highlighting or labeling the specific attribute of interest.



The *Virtual Human* comes equipped with an on-screen user's guide, installation instructions and the *Virtual Human Atlas* software package. Getting started from CD-ROM is relatively simple: the program opens to a title page with an easy-to-follow main menu. Learning the basic commands of the *Virtual Human* by trial and error proved to be a rather futile task. The online "Tour" command is the only way to fully appreciate the capabilities of the software. With each application, one begins by opening a status window that indicates the speed at which the software is retrieving data. The conveniently located tool bar contains relatively few, easy-to-use commands, such as rotate, resize, move, and identify. Once a dialogue box is opened, the user must begin to define the images they wish to view. The software divides the body into anatomical regions and systems. The anatomical subdivisions include head, neck, thorax, abdomen, upper and lower extremities, and pelvis. The system subdivisions include articulations, circulatory, digestive, endocrine, muscular, nervous, reproductive, respiratory, skeletal, and urinary. In order to view a particular image the user must specify an anatomical region and a particular system. For example, if one were interested in viewing the anatomy of the brachial plexus it would be necessary to select upper extremities and nervous system. With the click of a button the general anatomy of the brachial plexus is revealed.

The *Virtual Human* goes beyond the simple, run of the mill textbook viewing of images, by offering a host of commands that allow the user to fully appreciate the anatomy of the human body. The rotation, resize, and move commands enable the user to view the particular anatomical structure from all angles. Other ostentatious functions include the ability to highlight, hide or make various body parts transparent. These commands allow the user to specifically focus in on a select body part of interest without the distraction of other parts. Furthermore, a "Find" command exists to isolate those parts of the anatomy that are difficult to see at first but exist nonetheless. The *Virtual Human* software package also allows the user to alter the lighting of images, to label specific body parts as well as cutout sections of anatomy. Finally, images can be prepared for publication or exported to other programs with relative ease. The advantage of the *Virtual Human* is its ability to provide quick, easy access to a wide array of images. Problems with the software, however, do exist. In order to fully appreciate the images one must use a high-resolution image with oversampling. While this provides the best viewing, it is also the most time consuming. As well, the online instructions, a mandatory read, can at times be confusing and not straightforward. When all is said and done the *Virtual Human* proves to be a step in the right direction in the educational computer software field.

C : \ Quick \ Reference \ Review

Gold Standard Multimedia Inc.
http://www.gsm.com
List Price: $195 (US)
Rating (out of 5):***1/2

System Requirements:
Both PC and Mac are supported on the same CD
Windows - Pentium 100 MHz or higher, Windows 95 or NT, 32MB RAM
Macintosh - System 7.0 or better, Power PC 100 MHZ processor or better, 32MB RAM

The Doctor's Dilemma - Essentials of Medical Ethics

Brian Rotenberg, BSc. (OTO) and Eyal Cohen, BSc. (OTO)

As medical students, we are becoming increasingly dependent on computer-based technology as a mode of learning the enormous corpus of knowledge in modern medicine. At its best, computer-based learning provides easy-to-use formats to teach material in an interactive manner. Concepts are often easier to grasp because the technology appeals to multiple sensations: touch, vision and hearing. Multiple resources can also be tapped into at the touch of a button, without the irritating need to rely on burdensome indices.

At their worst, medical computer programs can be overly gimmicky, relying more on flare than substance to engross their users. Unfortunately, *The Doctor's Dilemma - Essentials of Medical Ethics* fits more into this latter category. The program is a poor attempt to grapple with the complexities of medical ethics within the construct of an interactive user interface. While the issues it tackles are diverse and salient to the practicing physician, its method of dealing with them, most notably via a wholly Christian-American point of reference, is deplorable.

In this educational CD-ROM the user plays the role of a family physician (male or female) undergoing a week of torturous ethical decision making. Faced with a variety of clinical encounters (e.g. DNR orders, abortion, confidentiality, suicide, alternative therapies and malpractice) the user has the ability to consult with various professionals: a psychologist, an ethicist, physician(s), a religious leader and, of course, a lawyer (this is an American program after all!). Links to textual resources (published guideline statements, government regulations, position papers) are provided to help you make a sound ethical decision. The program guides you through a series of 'conversations' with the patient and with the consultants, and allows you to examine the resources, as it displays a huge array of information on which to base your choice. It then presents you with feedback on your decision and asks you to consider the various implications of the action (or inaction). Finally, you commit and the resolution is presented. Throughout the process a myriad of difficult/important terms are defined, and references for further reading are given.

The consultants form the majority of the decision making aids (the textual resources, while a good source of information, are too detailed to be of real use); hence, it is worthwhile to dissect them further. 'Conversations' with them are useful and realistic, but in this case realism might have been sacrificed to make a more succinct program. In general the consultants are very chatty about irrelevancies and as they present arguments for their viewpoints, it is very easy to get lost in the details. While this may also be a good description of ethics in general, it must be said that a simpler series of conversations would indeed simplify the learning as well. Finally, the physician/colleague, who in real life would likely be the first consultant most doctors would turn to, is represented by a crass individual with no insight into ethical matters; despite physician colleagues being one of the most important links in the chain of an ethical decision making process, this particular consultant is by far the weakest.

Unfortunately, the database also reflects a surprisingly narrow value system. On the issue of euthanasia, we found a link to religious views on euthanasia. In it there were the views of thirteen different Christian sects on assisted suicide and nothing from any other of the major world religions! This may reflect the predominance of Christianity in Georgia (where the program originated), but it limits the application of the program to more heterogeneous populations of practicing physicians as may be found in Toronto. Similarly, the legal links and consensus statements were solely American in origin and had little or no applicability to any non-American physician.

The Doctor's Dilemma is a valiant attempt to try to address the teaching of ethical issues by computer. We believe it is also a dismal failure. Unlike other medical topics, ethics is best learned in group settings with one's professional colleagues. These sessions can be called seminars, Problem Based Learning or anything else, but what they do best is let students think through the process that is involved in making an ethical decision in a small group setting with students from a varied educational and socio-cultural background. *The Doctor's Dilemma* fails in this regard because it does not deal with ethical issues from a diverse perspective and because it fails to reproduce the interactive elements of group decision making and consultations in ethics.

Is there anything good about the CD? As mentioned earlier, it presents a wealth of textual information and references for difficult terminology. As well, it has a wonderful index listing all of the terms used, so it is useful as a quick guide for definitions. The best aspect, however, is that throughout the program one is forced to reflect on his/her own thoughts and decision making algorithms, and examine their appropriateness. In this sense the CD does accomplish one of its goals, that of giving one insight into his or her personal viewpoints and strategies. However, unlike anatomy atlases, heart sound tutorials, or other medical topics, realistic ethical problems seem to be colourful enough in their own right that they do not need the pictorial supplementation of a CD-ROM to maintain the student's interest.

C : \ Quick \ Reference \ Review
Gold Standard Multimedia Inc.
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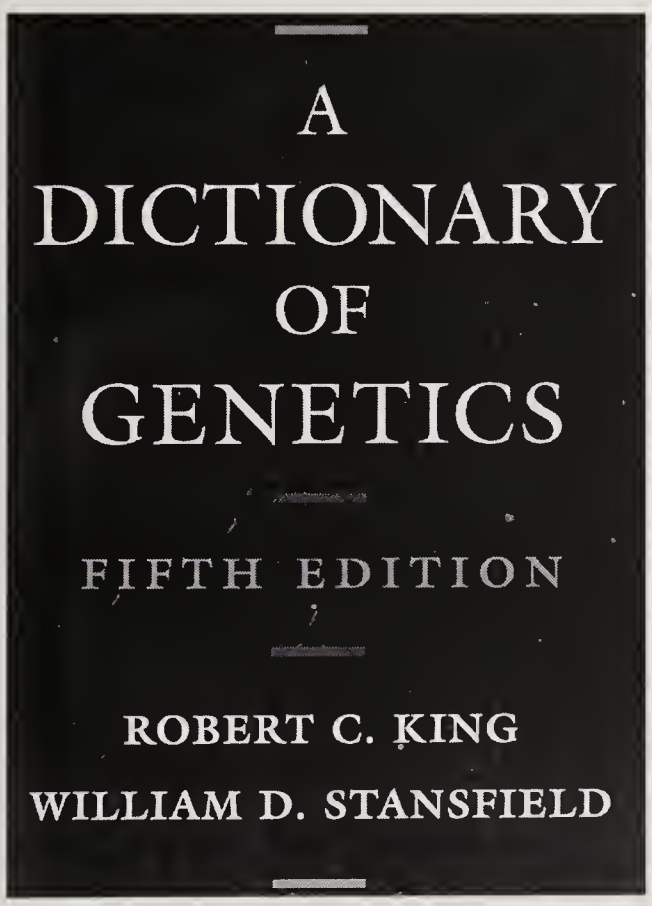
A Dictionary of Genetics

Reviewed by Richard Bitar, MSc. (0T1)

Written by Robert C. King and William D. Stansfield
Oxford University Press, 5th Edition, 1997
Pages: 439

Overall Rating:	Excellent
Strengths:	Comprehensive yet concise, cross-references information
Weaknesses:	While it provides literature citations, only the author's names and year of publication are supplied
Audience:	Students (especially those with an interest in genetics and molecular biology), geneticists



Genetics is one of the fastest advancing fields of the life sciences. Such growth is accompanied by a proliferation in terminology, and this terminology often represents a problem to the beginning students and to scientists from other disciplines who read genetic papers.

King and Stansfield provided a dictionary of genetics that is broader than what its name implies. Besides defining strictly genetics words, it also describes non-genetic terms that are often encountered in genetic and even medical literature. In addition to this, it also includes molecular and cell biology terms, which normally would not be found in conventional dictionaries of biology.

There are a variety of things which I liked about this dictionary. The definitions are very comprehensive, while remaining concise. Many of the terms are cross-referenced to one another, either for further explanation or so that they can be contrasted. For example, when the term *translation* is defined, it is cross-referenced to other terms such as *amino acid, elongation factor, N-formylmethionine,* and *peptide bond,* all of which help to further the understanding of the process of translation. However, it is not essential to read the other terms since the definition of translation by itself is extensive. Another example is the definition of *T lymphocyte,* where the authors cross-reference it with the term *B lymphocyte,* so that the reader can see the difference between these two cell types.

Many of the diseases that have a genetic component associated with them are described in this dictionary. Some examples are sickle cell anemia, familial hypercholesterolemia, familial amyotrophic lateral sclerosis, epidermolysis bullosa, and cystic fibrosis. In the case of cystic fibrosis, the definition of this disease comprises its incidence, the way in which the disease is inherited, and in which gene the mutation leading to cystic fibrosis occurs. In fact, it goes as far as telling the reader that the majority of the mutations in the CFTR protein are delta-F508, describing that "the abbreviation indicates that there is a deletion (delta) of phenylalanine (F) at position 508." It even includes a diagram of the CFTR protein.

Another aspect of this dictionary which I quite enjoyed was the referencing of information to primary literature. In Appendix C, a chronological listing of some of the most important discoveries and inventions that have led to great advances in the various fields of the life sciences is presented. This list is cross-referenced to the various definitions of the dictionary. For example, the definition of *Polycystic Kidney Disease,* which cites the paper by Hughes *et al.* (1995), details the complete nucleotide sequence of the gene PDK1, and the mutation which causes the disease. However, only the names of the authors and the year of publication of the citation are provided. It would have been better to include the full citation, making it easier for the reader to search for an article if the reader wishes to do so.

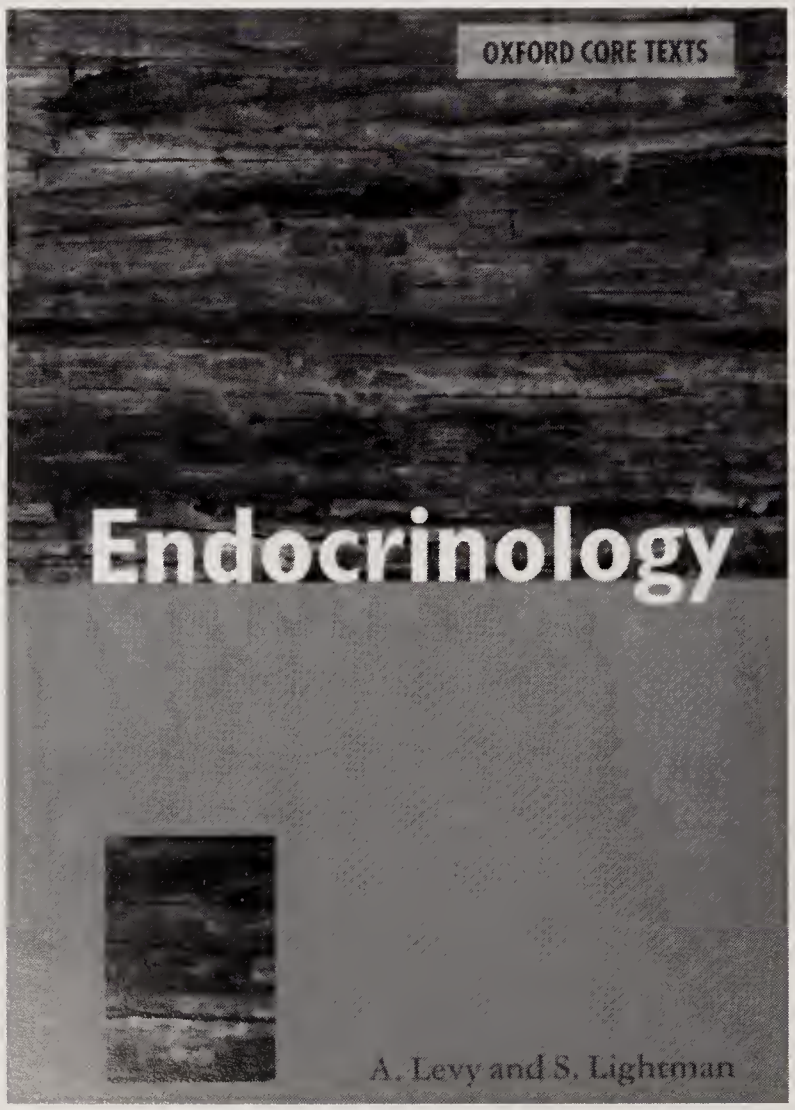
In summary, I strongly recommend this book since it does a great job of defining a variety of genetic and non-genetic terms in an easy and understandable way.

Endocrinology

Reviewed by Kristen Gyetvai, BSc. (OTO)

Written by S. Levy and S. Lightman
Oxford University Press, 1997
Pages: 397

Overall Rating:	Good
Strengths:	Simplified approaches to investigation, description of feedback loop systems, clinical scenarios
Weaknesses:	Lack of additional references
Audience:	Medical students



Endocrinology by Levy and Lightman attempts to bring endocrinology to medical students in a concise and understandable manner. This textbook begins with an introductory chapter providing a short review of the types of hormones and their mechanism of action. Although not as thorough as a classic physiology text, it provides enough information to "dust off the cobwebs."

The following chapters comprise the meat of the book. Each chapter begins with an outline of the normal function of the gland being discussed, followed by typical pathology and a sample clinical scenario. The emphasis is always placed on the most common pathology, with only a passing mention of the rarities. There are numerous coloured figures throughout to explain the various feedback loop systems which exist. Chapters are also accented with well-designed schemes that provide an approach to the investigation of selected disorders.

In addition to chapters focusing on each of the body's major glands, there is a chapter dedicated to common clinical complaints such as amenorrhea, diabetes, and hyperlipidemia. There is also one chapter devoted to the explanation of laboratory investigations. This includes the indications for the tests, methods of testing, and how to interpret the results.

The chapters are concluded with at least one relevant clinical scenario to test your clinical reasoning. Multiple choice questions are available and are accompanied by a full explanation to highlight the main points of each chapter.

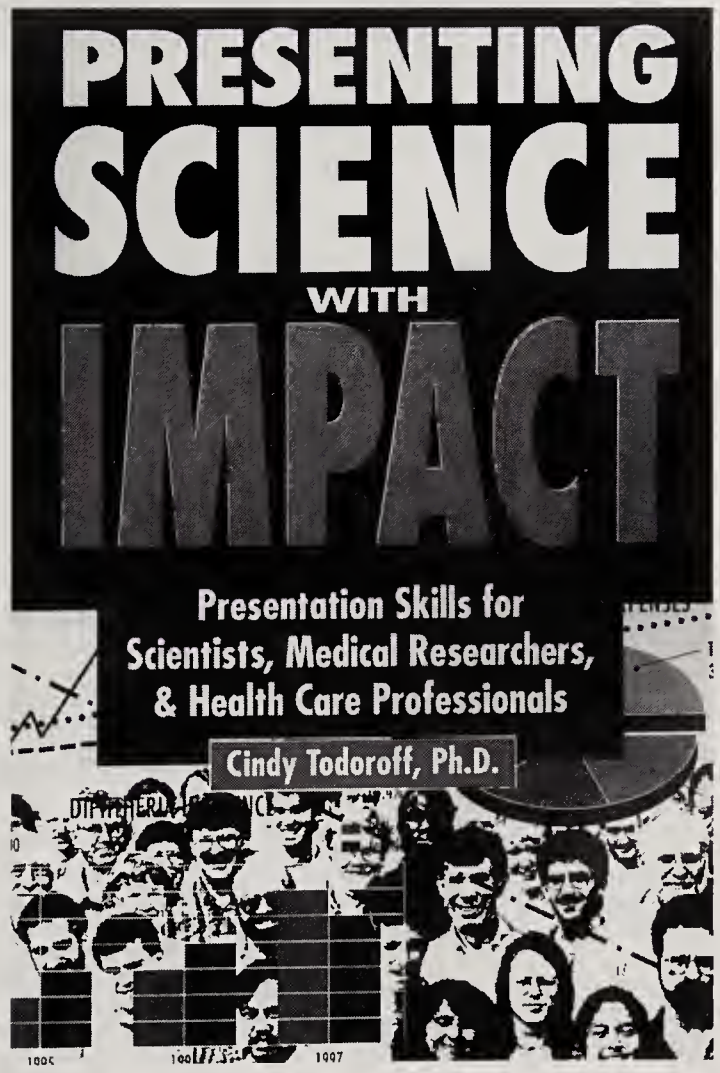
A drawback to *Endocrinology* is the lack of additional references for those who wish to pursue a topic in more detail. In summary, *Endocrinology* provides a clinically focused overview of what can be a complicated specialty. Although lacking in intense physiology, it provides clinical applications which are explained in a concise and understandable manner.

Presenting Science With Impact

Reviewed By Lilia Malkin, BSc. (0T1)

Written by: Cindy Todoroff, Ph.D
Trifolium Books Inc., 1997
Pages: 116

Overall Rating:	Excellent
Strengths:	Concise, well organized, and easy to read. Offers practical advice on all aspects of presentation delivery. Excellent sections on verbal/non-verbal communication and Q&A period. Good review of visual aids. Helpful charts summarize information
Weaknesses:	Section on presentation graphics software somewhat detailed; summary chart compares only the older software versions
Audience:	Health care professionals, medical and basic science researchers, science students, and general public



When one is called upon to give a talk, one hopes to impress the audience with the clarity, creativity, and general excellence of the presentation. Unfortunately, presenters often realize too late that their performance fell short of those expectations (i.e. after the presentation). *Presenting Science With Impact* helps avoid such disappointments by serving as a practical guide to delivering the kind of presentation that is eagerly anticipated by all audiences.

As Dr. Todoroff points out in her introduction, presentations form an integral part of any academic or medical career. Her book provides an excellent roadmap to all aspects of creating a successful presentation, from the initial stages of choosing an audience-appropriate topic to the conclusion and the inevitable Q&A period.

Several aspects of this work combine to make it a highly useful reference text. Primarily, the book is written in a clear, concise, and highly readable manner. Its brevity is one of its best features, making it accessible to the busy physician, researcher, or science student. The author's common-sense, direct writing style, combined with the large type font, contributes to quick reading and rapid assimilation of information. Moreover, the book is

very well organized, allowing a step-by-step approach to presentation design and delivery. Finally, this text is comprehensive, combining useful information on topics ranging from Visual Aid Selection to platform and delivery skills.

The chief value of this publication lies in its dual perspective: the components of a successful presentation are shown both from the speaker's and the audience's positions. One of the book's highlights is the incorporation of presentation scenarios at the beginning of every chapter, which demonstrate the "do's" and "don'ts" of presenting in a practical setting. Everyone, who has ever given or attended a presentation, be it formal or casual, will recognize themselves either as the flailing speaker or the unfortunate audience member. This technique allows the reader to visualize the consequences of different approaches to presentation preparation, stressing the importance of the topic covered in the chapter.

Other commendable features of the book include comprehensive coverage of presentation Preparation, Visual Aid Selection, Design, and Use, as well as Delivery Skills. Helpful summary charts that allow the reader to view the pros and cons of each medium accompany the section on Visual Aids. Current multimedia technology and presentation software are reviewed in a highly readable fashion. Practical tips on voice projection and body language are highlighted in the chapter on Platform and Delivery Skills. The Q&A Period section shows the reader how to handle the audience's questions in a calm, constructive, and professional manner, to ensure that the presentation remains effective to the very end.

Finally, the chapter-end exercises make up yet another praiseworthy feature of this text. The exercises allow the reader to design a presentation from start to finish – in an organized and constructive manner. This is valuable to new and experienced presenters alike, as the exercises are designed not only to learn new presentation skills, but also to improve existing ones. The reader learns both the basics and the subtleties of creating well-organized, clear, creative, and, most importantly, target audience-tailored presentations.

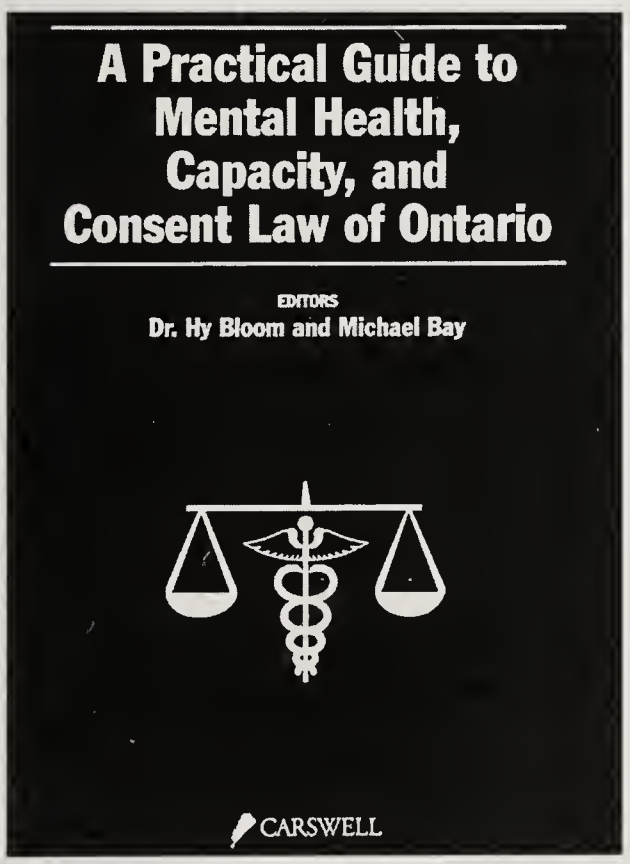
Presenting Science With Impact provides a sound template for consistently excellent delivery of high quality presentations. As Dr. Todoroff concludes, "Best wishes for every upcoming presentation!"

A Practical Guide to Mental Health, Capacity, and Consent Law of Ontario

Reviewed by Chris McIntosh, MSc. (OT1)

Edited by: Dr. Hy Bloom and Michael Bay
Carswell, 1996
Pages: 582

Overall Rating:	Excellent
Strengths:	Invaluable content, and superb organization; easy to read
Weaknesses:	Weak glossary; some chapters a bit dry
Audience:	Health-care professionals, lawyers



This book is a shining example of the proper way to compile a reference volume. As the title suggests, the book is a guide to the laws of Ontario that concern mental health, capacity and consent. Its nine chapters address such issues as: informed consent, powers of attorney for personal care, substitute decision-makers, maintaining patients in the community, involuntary hospitalization, liability, nursing issues, and confidentiality.

This small, lightweight volume is extremely well-organized. Each chapter is clearly structured with layered headings and subheadings, so that it is very easy to find information on specific issues simply by browsing through the table of contents. The index is also very useful in this regard.

The authors are all either health-care professionals or lawyers, and some of them are both. Remarkably, considering the subject material, the editors have managed to maintain a consistently readable style through most of the book. Important points are often illustrated by citing examples from actual legal and medical cases. Legislation is interpreted with a minimum of legal jargon, although I did occasionally stumble onto a Latin legal term which did not appear to be defined in the book's glossary.

The practicality of the guide is its most admirable feature. Academic discussion of medical or legal issues is kept to a minimum and in its place are specific suggestions for how to handle everyday medico-legal problems such as: how to obtain informed consent from an adult, a minor, or an elderly patient; how to manage the admission of an elderly patient to a long-term care facility; how to deal with consent and capacity issues in an emergency situation; how to keep proper medical records, etc. In addition, there are very interesting discussions on how to give expert testimony in court, how to avoid liability using preventative measures, and how to get along with lawyers.

The many appendices are a valuable addition to this book. One of them contains reproductions of all the forms you need to submit to the Ministry of Health or the Consent and Capacity Board to take action under the *Health Care Consent Act, the Substitute Decisions Act,* or the *Mental Health Act.* Another appendix contains flow charts and decision trees to aid in making judgements about a patient's medical capacity or dangerousness. Yet another appendix presents twenty-one common misunderstandings about consent and capacity legislation as they apply to elderly patients.

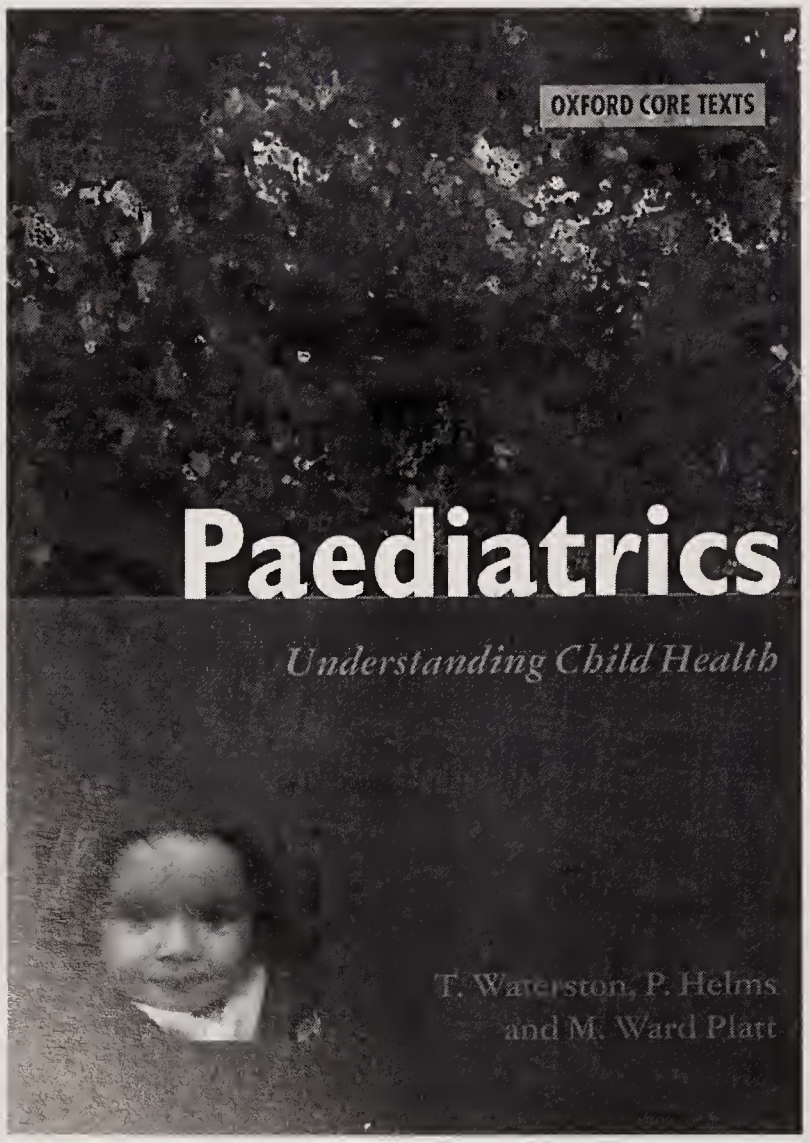
In summary, this book would be a valuable reference guide for all health-care professionals, particularly those with significant psychiatric components to their practice. It is specifically written for those without much legal expertise, but would nevertheless also be of use to lawyers handling mental health care cases.

Paediatrics: Understanding Child Health

Reviewed by Jason Pennington, MSc. (OTO)

Edited by: Tony Waterson, Martin Platt and Peter Helms
Oxford University Press, 1997
Pages: 422

Overall Rating:	Very Good
Strengths:	Useful tables and summaries of major points Good integration of multi-disciplinary management of childhood disorders
Weaknesses:	Limited to more common conditions
Audience:	Medical students



Following the miracle of birth, the tasks of growth and development are far from complete. During infancy, one is dependent on parents and other caregivers for all necessities of life. This period of rapid growth and development of motor and sensory systems allows infants to continuously learn about their bodies and how to interact with the surrounding physical and social worlds. Every infant adapts to its new environment in an individual and unique manner. There is therefore a wide range of normal growth and development during this period. Even so, failure to meet expected milestones, besides being potentially distressing to parents, may also indicate the presence of underlying physical, mental and social deficiencies. Meanwhile, an immature immune system is also developing and is soon barraged with a plethora of new pathogens. Childhood begins a period of supervised investigation of the world. This inevitably leads to dangerous acts and accidents (the number one killer of children above the age of one year). Increased social interaction with peers, necessary for developing skills required to interact in modern society, increases exposure to childhood diseases. Adolescence is associated with the physical changes of sexual maturation. It is also a period of great psychological change as one begins to define self and a role as an autonomous figure in society. Parental figures have played an integral role, having accompanied their child through all of these stages, and their concerns

and questions must be dealt with in an appropriate manner. This is the complex realm of paediatrics.

Paediatrics: Understanding Child Health was written with a great deal of insight into the needs of both the paediatric patient and the medical student for whom this text was intended. This book was not intended to give long differential diagnoses or to outline every rare condition one might encounter in a tertiary care facility. Using a holistic, child-centred model of health care, it gives the reader a good perspective of paediatrics from a primary care point of view. The information is presented in the form of clinical case studies with further discussion of relevant findings and considerations. Major points are highlighted in tables and summary boxes.

Section A comprises the first seven chapters and is dedicated to the current state of child health in modern society, along with the roles of epidemiology, prevention and the multi-disciplinary health care system in meeting the physical, psychological and social needs of this population. The lack of excessive technical epidemiological jargon combined with enlightening statistics and practical case studies were a very effective format for presenting the various social and environmental factors involving youth (including poverty, abuse and disabilities), and how they may manifest in clinical situations. Multi-disciplinary models for management are promoted and outlined. One of the minor drawbacks is that all of the statistics and allied-health services provided are based on the British model. This should not deter the reader in that most major health concerns are similar in all Western countries and one would have to investigate local services and practices regardless. The concepts are the essential information. For example, the second chapter, *Setting priorities: epidemiology in child health,* was especially insightful in providing many concrete examples as to how one might utilize population statistics to formulate relevant local studies in order to better understand and meet the health concerns of the population one is servicing, an important topic which is generally poorly covered by the medical school curriculum.

Section B, which contains the remaining seventeen chapters, provides an overview of situations leading to potentially precarious health (birth, accidents and poisoning), and a system-by-system examination of the common conditions contributing to childhood sickness. The information throughout this section is concise, and important differentials and clinical findings are usually conveniently summarized in tables and summary boxes. The differentials are normally made on the basis of prevalence, as opposed to an etiological or anatomical basis, as witnessed in the primary care setting (although one wonders why mitral valve prolapse was not mentioned in the section on congenital heart defects). Thus, zebras such as Gaucher's and specific mitochondrial genetic disorders are not included. The general format is to introduce the reader to some very basic concepts about a certain group of related conditions and then to present case studies which illustrate common clinical findings, emphasizing those that would indicate immediate intervention or require referral to specialists. The basics of management are covered with an emphasis on the patient, the family and the multi-disciplinary team. Once again, useful summaries are often provided.

In addition to tables and summaries, the text is accompanied by various figures and some flow charts. Some of the figures illustrate valuable concepts while others are incorporated for a predominantly aesthetic value. The text is very easy to read, and concepts and terminology are geared towards medical students. For this reason many of the topics are not explored in great detail or depth. One would have to make use of the references provided at the end of each chapter in order to obtain more specific (e.g. pathophysiological or pharmacological) details.

This text is not meant to replace Nelson's *Textbook of Pediatrics.* At a fraction of the size and containing only a fragment of the information, *Paediatrics: Understanding Child Health* is meant to compliment such texts. It provides medical students with a realistic concept of how the information contained in a purely medical text actually presents as a patient in a primary care facility. Also included are numerous practical examples and explanations as to how the biopsychosocial model can be incorporated into the primary care practice in an attempt to provide better health care to individual patients and the community at large. I recommend this book to any first or second year medical student who is still wondering how current courses will come together in clinical practice. Particularly those students with an interest in general paediatrics or any branch of medicine involved with primary care of children, may gain some practical insight from this information which is presented in a comfortable format.

UTMJ
University of Toronto Medical Journal

INSTRUCTIONS TO AUTHORS 1998-1999

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Contributions should be addressed to: The Editors, *UTMJ,* Medical Sciences Building, Room 2141, 1 King's College Circle, University of Toronto, Toronto, Ontario, M5S 1A8, Canada; Phone: (416) 946-3047. The paper should be submitted by an author, preferably the principal author, who should indicate in a covering letter:

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2. the exact address to which all related correspondence should be sent and the telephone and FAX numbers at which the author can be reached;

3. that neither the submitted manuscript nor any similar paper, other than an abstract of preliminary communication, has been or will be submitted to, or published, in any other primary scientific journal;

4. that all of the authors are aware of, and agree to, the content of the manuscript and that authorization has been given to use any information conveyed by either personal communication or release of unpublished experimental data;

5. three to six key words describing the paper, to assist in the selection of the reviewers.

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1. Reinders FX, Chalin C, and Meier HMR. (1993). Alzheimer's disease: Understanding the patient and caregiver. *UTMJ.* 70(20): 16-20.

* Abbreviated journal titles should be used.

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Article in a book or comparable publication

2. Norris KE, Norris F, and Brunfeldt K. (1980). *Nucleic Acids Synthesis: Applications to Molecular Biology and Genetic Engineering.* Koster H (ed). IRL Press: London, pp. 233-241.

Books, theses, or comparable publications

3. Pressaco J and Yu H. (1996). *Pharmacological Treatment of Diseases.* Urban Angel Medical Books Inc: Toronto.

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Both non-proprietary (generic) and trade names should be provided for all drugs mentioned.

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UTMJ
University of Toronto Medical Journal
Founded In 1923 Volume 75, No. 3 May 1998

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Dissection and Repair of Ulnar Nerve

1

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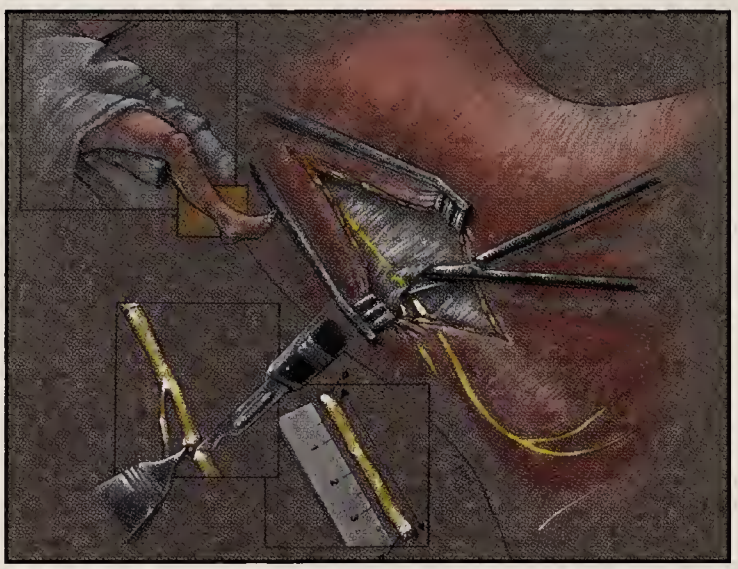

3

4

1) Patient orientation and location of ulnar nerve

2) Dissection of ulnar nerve

3) Dissection of sural nerve

4) Suturing of sural nerve to ulnar nerve

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